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Explanatory Models in Behavioral Endocrinology

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EXPLANATORY MODELS IN BEHAVIORAL ENDOCRINOLOGY

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Dissertation Abstract

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The historical development of explanatory models in the field of behavioral endocrinology, the study of hormones and their effects upon body and behavior, exemplifies both the philosophical account of scientific explanation by unification and mechanism. However, an examination of the reasoning behind the proposal and adoption of these models demonstrates that neither philosophical account can fully explain the development of the field.

Specifically, the development of the field is due to "crucial resolutions," resolutions of conceptual problems proffered and accepted in advance of unambiguous empirical evidence. Crucial resolutions decide between one or more elaborated hypotheses – hypotheses that can explain some (but not all) of the empirical data. While both the unification and mechanistic accounts can explain aspects of the adoption and development of the field, neither can account for the logic of discovery behind crucial resolutions.

The first chapter is a historical introduction to the early development of the field, focusing on the importance of the explanatory promise of hormones. Those chemical substances ('hormones') thought to be responsible for male and female developmental endpoints were gendered from the outset, and remain so to the present. From an initial, heuristic definition, hormones came to be defined as members of a specific chemical class.

The second chapter is an introduction to crucial resolutions in general, and an exploration of one resolution in particular: whether mammalian sexual development requires one hormone or two. The crucial resolution of this debate – that of the freemartin problem – determined the conceptual landscape for the future of the field.

The third chapter begins with a discussion of the philosophical debates concerning the possibility of a logic of scientific discovery. I demonstrate that, rather than being capricious, the process of discovery behind the formulation of elaborated hypotheses and the crucial resolutions that decide between them are founded on good reasons. This logic of discovery influenced the experimental confirmation of the crucial resolution, and not simply in terms of the initial questions investigated. I address this in the second half of this chapter.

After the question about the relative importance of male and female hormones for physiological development was resolved, the next general research program was to determine the etiology of sexual behavior. The general question addressed was whether mammals are inherently capable of demonstrating behavior typical of either sex, or if there is an "inequality of potential." The fourth chapter elucidates the arguments in support of the former claim, and provides historical background of the lines of thought leading to the triumph of the latter.

The fifth chapter details the research leading to the adoption of the dominant model of psychosexual development within the field of behavioral endocrinology: the organization/activation model, wherein prenatal gonadal hormone exposure permanently organizes the brain as either masculine or feminine. Hormones secreted in adulthood "activate" the previously organized tissues to induce masculine or feminine behavior. The scientific community initially adopted this model in part, because it promised to unite a wide range of phenomena under one explanatory model.

The organization/activation model was adopted by the scientific community with astonishing rapidity, not just because of its unificatory appeal, but because it provides a crucial resolution to an outstanding etiological mystery: that of homosexuality. According to the model, abnormal prenatal gonadal hormone exposure results in a brain whose "gender" is at odds with a phenotypically normal body. Chapter six presents the early, unsatisfactory hypotheses, both endocrinological and psychological, of the etiology of homosexuality, and how the organization/activation model appeared to provide a

satisfactory solution. Although, when first proposed, the model had no empirical evidence in support of its theory of human (male) homosexuality, it inspired a research program dedicated to uncover neurological gender atypicality.

The organization/activation model purports to explain the development of both normal and deviant types by reference to a single causal mechanism. The structure of explanation is as follows: the model plus one set of initial conditions yields a normal individual; the model plus another set yields a deviant individual of type T. This general explanatory model serves to explain not just normal physical and behavioral development (including sex differences in aggression and cognitive abilities), but also the emergence of homosexuality, transsexualism, and gender-atypical behavior correlated with endocrine abnormalities. As such, it appears to be an example of what Kitcher calls "explanation by unification." This is the topic of the seventh chapter.

In the eight chapter, I demonstrate how behavioral endocrinology fulfills the criteria for mechanistic explanatory models. As is the case in other areas of science, many endocrinologists *explicitly* describe their work as the search for underlying causal mechanisms. For the purposes of my argument, I focus on neurological investigations into the mechanisms underlying sexual and gendered behavior. While the organization/activation model is genuinely explanatory (if not always correct), mechanism cannot account for its rapid acceptance and uncritical extension to human gendered and sexual behavior.

One such uncritical extension is the topic of the ninth chapter: transsexuality. I begin with a historical introduction to early etiological hypotheses of gender identity, both "constitutional" and in terms of learning. With the crucial resolution of the etiology of homosexuality, the same general argument pattern was applied to transsexuality: a gendered brain incongruent with the body. There are two versions of this explanation of transsexuality. The first, that it is a variety of homosexuality, fails the criteria of genuinely explanatory mechanistic models. The second, that it is a phenomenon distinct

from homosexuality, demonstrates a flaw in unificationist appeals: the same general argument pattern is invoked to explain two different developmental outcomes.

Finally, I conclude that an investigation of the field through the lens of crucial resolutions reveals both the strengths and the weaknesses of the unificationist and mechanist accounts of scientific explanation, while providing a more complete account of the development of explanatory models.

Explanatory Models in Behavioral Endocrinology

Introduction

The historical development of explanatory models in the field of behavioral endocrinology, the study of hormones and their effects upon body and behavior, exemplifies both the philosophical account of scientific explanation by unification and mechanism. However, an examination of the reasoning behind the proposal and adoption of these models demonstrates that neither philosophical account can fully explain the development of the field.

Specifically, the development of the field is due to "crucial resolutions," resolutions of conceptual problems proffered and accepted in advance of unambiguous empirical evidence. Crucial resolutions decide between one or more elaborated hypotheses – hypotheses that can explain some (but not all) of the empirical data. While both the unification and mechanistic accounts can explain aspects of the adoption and development of the field, neither can account for the logic of discovery behind crucial resolutions.

As proving this claim will require a great deal of ground work, the first chapter is a historical introduction to the early development of the field, focusing on the importance of the explanatory promise of hormones. Those chemical substances ('hormones') thought to be responsible for male and female developmental endpoints were gendered from the outset, and remain so to the present. From an initial, heuristic definition, hormones came to be defined as members of a specific chemical class.

The second chapter is an introduction to crucial resolutions in general, and an exploration of one resolution in particular: whether mammalian sexual development requires one hormone or two. In other words, whether in feminine embryonic development the mere *absence* of male hormones suffices, or if specifically *female* hormones are required. The crucial resolution of this debate – that of the freemartin problem – determined the conceptual landscape for the future of the field. Importantly for my argument, the actual empirical results of the resolutions and crucial experiments generated by the research programs are often interpreted as supporting the crucial resolutions more strongly than the evidence allows.

Both the initial, plausible hypotheses put forth to explain the phenomena and the crucial resolutions that decide between them exhibit a logic of discovery, the topic of the third chapter. I present arguments both against and for the possibility of a logic of discovery, and present some examples from the history of endocrinology in support of its possibility. In addition, the logic of discovery – in the form of crucial resolutions – influences the logic of method, and not merely in terms of which problems are addressed. I demonstrate this using the example of the empirical confirmation of the crucial resolution mentioned above.

The fourth chapter addresses another crucial resolution in the history of behavioral endocrinology; one concerned with the etiology of sexual and gendered behavior. The general debate concerned whether all mammals have the potential to display both masculine and feminine behavior. That is, whether mammals, when born, have the capacity to display behaviors typical of either sex, or if there is an "inequality of potential" wherein animals are predisposed towards behavior specific to their anatomical

sex. Here, I elucidate the arguments in support of the former claim, and provides historical background of the lines of thought leading to the triumph of the latter.

The organization/activation model was adopted by the scientific community with astonishing rapidity, not just because of its unificatory appeal, but because it provides a crucial resolution to an outstanding etiological mystery: that of homosexuality. According to the model, abnormal prenatal gonadal hormone exposure results in a brain whose "gender" is at odds with a phenotypically normal body. Chapter six presents the early, unsatisfactory hypotheses, both endocrinological and psychological, of the etiology of homosexuality, and how the organization/activation model appeared to provide a satisfactory solution. Although, when first proposed, the model had no empirical evidence in support of its theory of human (male) homosexuality, it inspired a research program dedicated to uncover neurological gender atypicality.

The organization/activation model of psychosexual development appears to be, upon first glance, an exemplar of explanation by unification. In the seventh chapter, I demonstrate that it is such an exemplar, drawing primarily upon the work of Philip Kitcher. Many scientists have extolled this explanatory model for its ability to unify seemingly disparate phenomena – specifically, the embryonic phenotypical development of genitalia with neurological developments influencing hormone regulation, sexual and gender-related behavior, and cognitive abilities. However, the goal of scientists within this field has been, and continues to be, to cash out the initial predictions of the model in terms of biochemical mechanisms, an appeal to causality that explanation by unification cannot incorporate.

In the eighth chapter, I demonstrate how behavioral endocrinology fulfills the criteria for mechanistic explanatory models. As is the case in other areas of science, many endocrinologists *explicitly* describe their work as the search for underlying causal mechanisms. For the purposes of my argument, I focus on neurological investigations into the mechanisms underlying sexual and gendered behavior. While the organization/activation model is genuinely explanatory (if not always correct), mechanism cannot account for its rapid acceptance and uncritical extension to human gendered and sexual behavior.

One such uncritical extension is the topic of the ninth chapter: transsexuality. I begin with a historical introduction to early etiological hypotheses of gender identity, both "constitutional" and in terms of learning. With the crucial resolution of the etiology of homosexuality, the same general argument pattern was applied to transsexuality: a gendered brain incongruent with the body. There are two versions of this explanation of transsexuality. The first, that it is a variety of homosexuality, fails the criteria of genuinely explanatory mechanistic models. The second, that it is a phenomenon distinct from homosexuality, demonstrates a flaw in unificationist appeals: the same general argument pattern is invoked to explain two different developmental outcomes.

Finally, I conclude that crucial resolutions appeal to unifcatory ideals, but set the disciplinary matrix in terms of mechanistic explanations. As such, I suggest that what counts as an explanation in the field of behavioral endocrinology is not a case of the same phenomenon being explained in two different ways, one mechanistic and the other unificationist, but rather a single explanatory model that explains the phenomena in terms of a general, mechanistic schema. An investigation of the field through the lens of

crucial resolutions reveals both the strengths and the weaknesses of the unificationist and mechanist accounts of scientific explanation, while providing a more complete account of the development of explanatory models.

Chapter 1

The Importance of Hormones

I. Introduction

The discovery of hormones drastically changed the field of biology in general, and the field physiology in particular. In particular, it shifted the focus of research from external to internal factors. In what follows, I give a brief history of early research on hormones and their initial, vague, categorical definitions. These initial definitions were in terms of function, rather than chemical composition. For this reason, I begin my substantive discussion of endocrinological research in the early part of the 1900s.

Because the biochemical mechanisms operating in bodies were, at this time, unknown, initial discussions were framed in terms of internal versus external factors. To use the terminology of Wesley Salmon, these internal factors were “black boxes” whose internal workings, initially, are mysterious. The role of science is to open them up to see

how they work.[1] At this time, scientists identified three classes of internal factors: heredity, the nervous system, and what were labeled 'internal secretions.' Because the field of genetics was in its infancy, with the result that the question of how genes organize the nervous system was unanswerable, many researchers focused their investigations of internal factors on the (internal) secretions of the ductless glands. This narrowing of focus was not (merely) due to the seeming lack of immediate progress in the fields of genetics and neurophysiology; as I demonstrate, the burgeoning field of endocrinology itself held out great promise.

Because of the comparatively primitive laboratory techniques of chemical assay, the initially posited 'internal secretions' were defined in terms of their effects on nearby organs. In other words, their definition was functional, rather than structural. With technological advances in the field, the internal secretions came to be regarded as a particular class of chemical substances deemed 'hormones.'

The early, vague mechanistic explanations of hormones and their effects upon the body developed into research projects dedicated to elucidating the mechanisms of biological feed-back loops, as well as the more general project of determining the overall importance of hormones upon the functioning of the mammalian body including, importantly for my later claims, mammalian sexuality. But first, some intellectual background to set the stage.

II. Internal versus External Factors

[1] Salmon, W. (1998). The Importance of Scientific Understanding. Causality and Explanation. W. Salmon. New York, Oxford University Press: 79 - 91.

Before the development of endocrinology as a clearly defined subfield, the question of the relative influences of internal versus external factors was a question about the relative importance of the environment as opposed to that of genes (specifically, how they organize the nervous system). However, because the science of genetics was very young, researchers had only extremely vague hypotheses concerning the mechanisms by which genes determined physiology and behavior. As Naccarati and Garrett, in their 1923 paper on the comparative influences of 'constitutional' versus environmental influences on behavior, write:

> A growing organism is, in general, subject to the action of two systems of forces: the internal – those inherited through the germplasm – and the external – those residing outside of it in the environment. Of the two determinants, the second, being the most obvious, is usually assigned first place.[2]

Because behaviors and the environmental forces correlated with them are more easily observed than genes (especially at this time), most researchers focused upon, and hence gave more weight to, external factors. Investigations into learning, for instance, gave preeminence to the environment. Naccarati and Garrett note that this same state of affairs, that is:

[2] Naccarati, S., and Garrett, Henry (1923). "The Influence of Constitutional Factors on Behavior." Journal of Experimental Psychology **6**(6): 455 - 465.

> The greater importance of external factors as against the internal, may be observed also in medicine; the causes of disease are usually sought in morbid factors which enter the organism from without – germs, poisons, traumata.[3]

With the opening up of the internal "black boxes," the importance of external factors lessened with time. More accurately, with the development of the *potential* to open the black boxes of internal factors, the focus of research shifted from the (supposedly easily) observable to the (no longer completely) unobservable. One such class of "quasi-observables" was that of the internal, glandular, secretions within the mammalian body.

In the infancy of the field of endocrinology, some scientists[4] noticed that some organs secrete chemicals directly into the bloodstream (not through the medium of ducts) that have transformative effects upon other organs and tissues in the body. This discovery challenged the then-common notion that the nervous system, and only the nervous system, was responsible for the development and maintenance of other organs.[5]

As Naccarati and Garrett point out:

> It has only been since the development of endocrinology as a branch of medicine that a better understanding of another important group of morbid causes, viz., the

[3] Ibid.

[4] For instance, A. A. Bertold, Claude Bernard, and Chareles Brown-Séquard.

[5] This notion of internal regulation is expressed concisely by Cuvier: "Le système nerveux est, au fond, tout l'animal, les autres systèmes ne sont la que pour le servir." Quoted in Abel, J. (1915). "Experimental and Chemical Studies of the Blood with an Appeal for More Extended Chemical Training for the Biological and Medical Investigator." Science **42**(1075): 165 - 178.

> endogenous, has been reached.[6] These causes, according to endocrinologists, are inherent in our organic makeup, in the more or less solid structure of our body, in the variable functional capacity of individual organs whether congenital or acquired during the period of development of the organism.[7]

That is to say, the investigation of internal factors – either hereditary or those "developmentally acquired" – not only could advance to field of palliative medicine, but that of biology in general.

The discovery of hormones held great promise for the fields of physiology and medicine. In particular, the secretions of the ductless glands promised to explain more aspects of physiology – especially those of sexuality – than could the nervous system per se, as well as appeals to the (then mostly conjectural) field of genetics.

Just as genetics did not appear to be a promising route of investigation at this time, the nervous system did not seem to be able to tell the whole story about behavioral responses in general and sexual behavior in particular. As a result, many investigators decided to persue the more promising route of hormonal research – especially in lieu of the rapidly advancing techiniques in chemical assays.

One proponent of the shift in emphasis from external factors in general to hormones in particular was Calvin Stone, who claims:

> No account of sexual behavior based wholly upon neurophysiology has been found adequate to explain the facts brought forward from experimental studies during the past thirty years. Hence new dynamogenic factors underlying sexual

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[6] "As Sir William Osler said recently, medicine has made no more brilliant advance than in the cure of certain diseases of these ductless glands." Kunkel, B. (1921). "Harmonizing Hormones." Scientific Monthly **13**(3): 266-274.

[7] Naccarati, S., and Garrett, Henry (1923). "The Influence of Constitutional Factors on Behavior." Journal of Experimental Psychology **6**(6): 455 - 465.

> activation have been sought. This search has led to investigations in the field of endocrinology with the result that data pertaining to a testicular hormone have been revealed which are of interest to students of behavior.[8]

For instance, the suppression and eventual extinction of sexual behavior in adult male castrates has been noted since antiquity. Some researchers explained this by claiming that castration cut the nerve connections from the testes to the peripheral muscles. However, this explanation is untenable in light the results of experiments wherein testes were implanted after castration and sexual behavior was restored.[9] As Stone points out, the explanation with the most experimental support:

> [I]s based on the assumption that the testes elaborates an internal secretion which, through its chemical influence on the nervous system and the general bodily metabolism, predisposes the animal to orient with respect to animals of the opposite sex and to carry out such further sexual responses as will eventually lead to the consummation of the reproductive act. The persistence of sexual behavior after castration is explained on the assumption that libidinous substances are retained in the blood for a variable period of time.[10]

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[8] Stone, C. Ibid."Experimental Studies of Two Important Factors Underlying Masculine Sexual Behavior: the Nervous System and the Internal Secretion of the Testis." (2): 85 - 106.

[9] See, for instance, Berthold, 1849.

[10] Stone, C. (1923). "Experimental Studies of Two Important Factors Underlying Masculine Sexual Behavior: the Nervous System and the Internal Secretion of the Testis." Journal of Experimental Psychology **6**(2): 85 - 106. Stone is careful to point out that:

> Factual data concerning the mode and seat of action of the testicular hormone are wanting. At the present time, however, it is generally believed that its influence is exercised by direct action upon the central and sympathetic nervous system and through chemical regulation of the general metabolism. The evidence upon which these assumptions rest, as we have shown, is indirect and conjectural, being founded primarily

While Stone did not ignore the importance of a properly developed nervous system, he rejected the notion that sexual behavior was "reflexive" (and thus completely dependent upon the nervous system) like other behaviors such as the 'scratch reflex':

> The copulatory response differs fundamentally from the 'scratch reflex' and other reflexes of similar nature by virtue of its dependence upon a special gland, the testis, for activation and regulation.[11]

This means that "instinctive" sexual responses were of a much more complicated character than reflexes solely dependent on the central nervous system. This initial, vague characterization of sexual response presages the complicated etiological picture that later emerges.

Once the scientific community accepted this system of regulatory internal chemical secretions as contrasting with and complimenting the (earlier) understood phenomenon of the nervous system, a new venue of investigation opened up. One early commentator writes:

> upon analogies taken from the actions of other hormones with which investigators are more intimately acquainted.

Stone, C. (1923). "Experimental Studies of Two Important Factors Underlying Masculine Sexual Behavior: the Nervous System and the Internal Secretion of the Testis." Journal of Experimental Psychology **6**(2): 85 - 106.

[11] Stone, C. (1923). "Experimental Studies of Two Important Factors Underlying Masculine Sexual Behavior: the Nervous System and the Internal Secretion of the Testis." Journal of Experimental Psychology **6**(2): 85 - 106.

> [I]n recent years we have come to understand that the complex of activities in the animal body is united into a functional harmony, not only through a reflex control exerted by the nervous system, but also by means of a chemical regulation effected through the blood or other liquids of the organism. The first serious realization of the importance of this second method of regulation came with the development of our knowledge of the internal secretions during the last decade of the nineteenth century.[12]

In addition, these scientists discovered that the chemical and organic interactions had a cyclical character – that is, internal secretions were not constant, but would ebb and flow according to distinct time periods. As a result, cyclical bodily functions were presumed to be controlled by a class of chemicals secreted by ductless internal organs. This (initially hypothetical) class of chemicals was given the name "hormone," and was accorded primacy in physiological research. Howell writes:

> There is thus established a *circulus benignus* by means of which each tissue profits from the functional activity of its fellow tissues. From many sides and in many ways facts have been accumulating which tend to impress the general truth that the co-activity of the organs and tissues may be controlled through chemical changes in the liquid media of the body, as well as through nerve impulses.[13]

This new emphasis on hormones ('internal secretions') led to a conception of the body "such that the products of metabolism in one tissue serve as a stimulus to the

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[12] Howell, W. (1910). "The Chemical Regulation of the Processes of the Body by Means of Activators, Kinases and Hormones." Science **31**(786): 93 - 100.

[13] Ibid.

activities of other tissues."[14] Scientists investigating the new field of hormones faced multiple (and exciting) challenges: determining the chemical nature of hormones[15], how many (mammalian) hormones existed, and uncovering the mechanics of each hormone-induced feedback loop.[16]

Unfortunately, techniques for chemical assays, as well as techniques of chemical isolation and refinement, were not advanced enough to identify any hormones except those few that were amenable to primitive techniques.[17] As time progressed, so did laboratory techniques, and thus the field of endocrinology.

Shifting the focus from genes to hormones promised to provide a more satisfactory explanatory model for some perturbations in development. For instance, for

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[14] Ibid.

[15] Abel, in his discussion of the initial determination of epinephrin, adrenaline, and suprerenin, claims that

> The actual finding of definite and specific chemical principles in the organs of internal secretions has in each case an importance in the way of explaining and correlating a large number of disconnected facts, only to be likened to the discovery of the etiological cause of an infectious disease.

Abel, J. (1915). "Experimental and Chemical Studies of the Blood with an Appeal for More Extended Chemical Training for the Biological and Medical Investigator." Ibid. **42**(1075): 165 - 178.

[16] See, for instance, Hoskins, R. (1924). "The Functions of the Endocrine Organs." Scientific Monthly **18**(3): 257 - 272.

[17] As late as 1931, investigators into the cortico-adrenal hormone had difficulties isolating their object of study:

> The method of Swingle and Pfiffner, although long drawn-out (taking usually 10 to 14 days) and offering many possibilities for the loss of potency to occur, is simple to carry out; that of Hartman takes only a few days but offers technical difficulties, particularly in the elimination of inert lipoid substances and of adrenalin.

Britton, S., and Herbert Silvette (1931). "The Cortico-Adrenal Hormone." Science **73**(1890): 322 - 323.

a pregnant female, an emotional shock could disturb her hormonal equilibrium, thus affecting the development of the fetus:

> Once the endocrine glands of the newborn begin to malfunction, its hormones will determine morphologic, neuro- and biochemical changes which will appear later on in the mature organism in a manner that will puzzle the most experienced psychologist if he wants to attribute the abnormal behavior to heredity and environment alone.[18]

Many researchers thought that an investigation into the effects of hormones (as opposed to the genetic ordering of the nervous system) could explain typical, not just atypical, development. This reflects the general approbation of Frank Lillie's focus upon the exceptional as a means of explaining the unexceptional, whose work is discussed in the following chapter.

III. From Function to Structure

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[18] Naccarati, S., and Garrett, Henry (1923). "The Influence of Constitutional Factors on Behavior." Journal of Experimental Psychology **6**(6): 455 - 465. The authors make a suggestion that is prescient of future investigations into the etiology of homosexuality:

> And since mental changes when due to endogenous causes connected with the endocrine glands are usually accompanied by morphologic changes or characteristics also (because of the influence which the hormones exercise on the morphogenesis as well as on the nervous system and the metabolism), therefore a systematic study of the morphologic type of a given individual should yield valuable information concerning his mental status also.

Naccarati, S., and Garrett, Henry (1923). "The Influence of Constitutional Factors on Behavior." Journal of Experimental Psychology **6**(6): 455 - 465.

During the early development of the field, endocrinologists identified hormones as chemical substances secreted by organs that induced changes in other organs – not as members of a specific chemical family, as is the common practice today. For instance, Howell (in 1910) lists the known internal secretions as carbon dioxide, adrenalin, bile, and "iodothyrin" of the thyroid gland. He also notes that:

> In addition there are a number of hormones of unknown composition which have been either proved or assumed to exist, and which are held responsible for certain well known correlations of functions.[19]

While all four of the above-mentioned substances are involved in biological feed-back loops, the notion of "hormone" eventually came to be associated with a specific class of chemicals excreted by ductless glands, among them the sex glands.

The infant field of endocrinology held great promise not just for medicine in particular, but for biology in general. In an early review, B. Kunkel writes:

> It is only very recently that the full significance of this last class of coordinators [what he refers to as "special chemical substances which modify different parts of the body"] has been realized and it is to this system that I would call your

[19] Howell, W. (1910). "The Chemical Regulation of the Processes of the Body by Means of Activators, Kinases and Hormones." Science **31**(786): 93 - 100. Interestingly, Howell cautions that it seems

> . . . probable that the term hormone, like some of the useful terminology of immunology, will be overworked, and that investigators may deceive themselves as well as others when they conclude that any given relationship is an example of hormone regulation.

Howell, W. (1910). "The Chemical Regulation of the Processes of the Body by Means of Activators, Kinases and Hormones." Science **31**(786): 93 - 100.

> attention specially. Within the past few years the energies of a great number of physiologists have been directed to certain specialized organs having the structure of glands but not communicating with any free surface by means of ducts. These organs secrete internally, directly into the blood stream from which they have derived the raw materials from which the hormone is secreted. The effects on neighboring organs of the products of other organs has been studied with great earnestness for some years, but our knowledge is still in its infancy.[20]

This functional definition of internal secretions (hormones) acts as an initial, heuristic, conception of the phenomena. As an example of this functional, rather than chemical, definition, Abel describes his use of the term "internal secretion" as follows:

> For the present we shall follow custom and apply the term *to definite and specifically acting indispensable chemical products of certain organs (organs that may or may not have an external secretion), which are poured into the blood and modify the development and growth of other organs, more especially during embryonic and early life, and which also greatly affect the entire metabolism, that of the nervous system included, during adult life.* (Original emphasis.)[21]

Scientists could describe the effects of some internal secretions (particularly those of the testes[22]), but could not yet *explain* those effects. As such, the over-arching goal in the field of endocrinology was to discover the number and nature of these hormones.

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[20] Kunkel, B. (1921). "Harmonizing Hormones." Scientific Monthly **13**(3): 266-274.

[21] Abel, J. (1915). "Experimental and Chemical Studies of the Blood with an Appeal for More Extended Chemical Training for the Biological and Medical Investigator." Science **42**(1075): 165 - 178.

[22] Even before they were determined to be ductless, the (male) gonads were considered an important developmental inductor:

This general, proto-mechanistic program of research echoes other historical incidents of scientific explanations. An example of this type of explanation, and the understanding that comes with it, is the work of Jean Perrin on Brownian motion – the behavior of microscopic particles in fluid. First discovered by the botanist Robert Brown early in the nineteenth century, Brownian motion remained a mystery until the first decade of the twentieth century, when Einstein published his famous paper on the topic, offering a theoretical explanation. Perrin's monumental experimental work confirmed Einstein's theory. Salmon notes that we should:

> Notice how we need to go to the submicroscopic level to explain microscopic phenomena, something that many physical scientists thought impossible at the turn of the present [20th] century. Not only did Perrin establish the mechanism of Brownian movement, but he also ascertained Avogadro's number, the number of molecules in a mole (gram molecular weight) of any given substance.[23]

This shows the hierarchical nature of mechanical systems, in that submicroscopic interactions can produce microscopic changes. In the case of endocrinology, the "submicroscopic" interactions are those of internal factors and bodily tissues.

> Man has long made practical use of the fact that the removal of the sex glands at a certain age will give us the docile ox in place of the unruly bull, the easily fattened and tender-fleshed capon for the muscular and stringy cock; and in human society in its various stages of development has also practiced this mutilation on its individuals for various reasons, religious, economic, or penal . . . From remote antiquity, therefore, man has known that the [male] gonads, or sex glands, exert a marked influence on the development and structure of the body.

Ibid.

[23] Salmon, W. (1998). The Importance of Scientific Understanding. Causality and Explanation. W. Salmon. New York, Oxford University Press**:** 79 - 91.

One way of "opening up" a black box is to hypothesize about the mechanics within it (as Einstein did in the case of Brownian motion). If the hypothesized mechanical system is sufficiently explanatory – to put it crudely, if it works – it can serve as a *model* for the relevant phenomena. Not only can it serve as a model, but it can serve as an explanatory model.

With technological advances in chemical analysis, it became apparent these hormones belonged to general chemical class. Once endocrinologists accepted the general notion that the substances inducing sexual differentiation were hormones, their task became to discover the number and nature of these hormones. Barker, in his discussion of the endocrine glands, notes that:

> The chemical substances contained in the incretions have been called "hormones" and the determination of the precise chemical constitution of these hormones sets fascinating tasks for the biochemist.[24]

Hormone research involved not just chemical analysis, but also deliberately interrupting or altering the normal process of development in order to determine the effects of excessive presence or absence of hormones on physiology.

While determining the number of hormones appeared to be a straight-forward task and, given advances in chemical analysis, relatively simple,[25] uncovering the nature of

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[24] Barker, L. (1922). "The Relation of Endocrine Glands to Heredity and Development." Science **55**(1435): 685 - 690.

[25] Collip writes:

hormones proved much more difficult. This difficulty was due, in part, to terminological vagueness, which in turn was due to a lack of understanding of the mechanisms underlying sexual development.

IV. Gendered Definitions

The development of endocrinology allowed scientists to investigate the influence of internal factors. These internal factors – later to be called "hormones" – were classified as chemical secretions of the ductless glands (also known as "internal secretions"). As such, the development of endocrinology allowed scientists to study the effects of hormones upon physiology and behavior. More specifically, hormones could work as the foundation for an explanatory model of mammalian psychosexual behavior.[26]

> It may be confidently expected that great advances will be made in this subject in the near future, because accurate methods for the assay of certain of the hormones in the blood and secretions of the individual are being developed.

Collip, J. (1936). "Hormones." Scientific Monthly **43**(5): 411 - 420.

[26] More than two decades after the work of Kunkel and Abel, William Perloff begins his review of the influence of hormones on human sexuality by stating that:

> The mechanism of sexual behavior has long been an intriguing although frustrating subject of investigation. With the discovery of the role of the gonads as producers of hormones, and particularly after the isolation, purification, and synthesis of the steroid hormones, biologists believed that a simple explanation of sexual behavior was at last available.

He goes on to note that, in spite of later, contradictory, observations, "the hormonal concept of sexual regulation is still widely held perhaps because of its apparent simplicity." Perloff, W. H. (1949). "Role of Hormones in Human Sexuality." Psychosomatic Medicine: Experimental and Clinical Studies **11**(3): 133 - 139.

As a result of the general acceptance of the (largely hypothetical) notion of hormones, it was a natural step to assume that the sex glands produced hormones. Indeed, male and female developmental endpoints were often thought to be the result of "male" and "female" factors present during embryonic development. For example, Conklin, in response to the general question concerning the "formative agent in embryonic [sexual] development," makes an initial suggestion that:

> Without attempting to find the *primum movens* we may conclude that if there are material differences in areas and cells it is not necessary to resort at once to some immaterial agent to account for their differentiation. It is impossible to understand, i.e., to make intelligible, development except as a result of the formation and localization of different material substances.[27]

In other words, physiological development can, and should, be explained by physiological substances. Specifically, different (sexual) developmental endpoints could be explained through appeals to different (gendered) material substances. Hormones, then, were defined functionally and in a gendered fashion. For instance, the "male hormone" was that chemical which, when secreted from the male gonads, controlled or determined specifically male characters in the organism.

Because the initial discussion of the factors divided them into male and female, subsequent discussions of the hormones also divided them into male and female. One result of this was less than ideal terminological distinctions between the chemical compounds (e.g., "estrogen" and "androgen"), organs of origin (e.g., "ovarian" and

[27] Conklin, E. (1933). "Mosaic vs. Equipotential Development." American Naturalist **67**(711): 289 - 297.

"testicular") and gendered ("male" and "female") hormones. Perloff, in his discussion of the role of hormones in human sexuality, notes that while estradiol "has been called the female sex hormone" and, likewise, testosterone "has been called the male sex hormone:"

> This terminology is unfortunate, because it suggests incorrect concepts and leads to faulty reasoning. As a matter of fact, the stallion produces more estrogenic material than any other animal known, and had it first been isolated in this animal, might very well be called the male sex hormone.[28]

These distinctions are less than ideal because a) both kinds of organs produce both kinds of chemical compounds, as a result of which b) neither compound can be correctly labeled as "male" or "female."

In spite of these ambiguities, endocrinologists were certain that "sex" hormones were responsible for developmental sexual physiology. The challenge remained to uncover the mechanisms responsible for specific developmental endpoints.

Once scientists accepted the existence of "male" factors and "female" factors, the question arose of their relative contributions to physiological development. Goldschmidt, in his discussion of intersexuality, writes:

> The embryological problem of intersexuality is then to find how the sex-determining hormones interact with such developmental processes which lead to sexual differences. Undoubtedly the developmental system concerned in the production of intersexuality has two phases: the inductive agency for which we use the term hormones, and the reacting tissues of the developing animal. The

[28] Perloff, W. H. (1949). "Role of Hormones in Human Sexuality." Psychosomatic Medicine: Experimental and Clinical Studies **11**(3): 133 - 139.

first question is, therefore, whether we are dealing with two inductive stuffs for the two sexes respectively or only with one.[29]

The etiological question of one or two hormones and its resolution is the topic of chapters three and four.

At this point in time, another question arose: are hormones *solely* responsible for the development of sexual behavior? Stone was convinced not only that hormones were necessary for sexual behavior, they were, given proper anatomic and neurological development, sufficient. From his studies of the differences between the sexual behavior of pre- and post-puberty castrates, he concludes that "the gonads are absolutely necessary for the completion of the development processes underlying overt expression of the sexual libido."[30] Not only are hormones necessary, Stone later suggests that "hormones form the *sine qua non* for the organization of sexual behavior in young vertebrates."[31] Here, Stone is making a stronger claim – not only are hormones necessary for the foundational processes that *support* sexual behavior, they are responsible for the organization of the behavior *per se*. In other words, while the development of mature sexual behavior cannot proceed without the presence gonadal hormones, the very

[29] Goldschmidt, R. (1938). "Intersexuality and Development." American Naturalist **72**(740): 228 - 242.

[30] Stone, C. (1932). "The Retention of Copulatory Ability in Male Rabbits Following Castrations." Journal of Genetic Psychology **40**: 296-305.

[31] Calvin Stone, "Sex Drive," in Sex and Internal Secretions, 2nd ed., 1939.

presence of gonadal hormones is sufficient for the development of adult sexual behavior.[32]

In spite of the simple appeal of this causal story, not all researchers thought that hormones alone were the causal agents behind mature sexual behavior. Frank Beach (who is discussed more thoroughly in the fourth chapter) pointed out that there are several lines of evidence implying that, while hormones were necessary, proved that they were insufficient.

One such line was observations of mating behavior in animals with a congenital lack of gonads. In particular, one researcher observed mating behavior in male pigeons that congenitally lacked testes.[33] Beach himself noticed a female rat, also congenitally lacking gonads (and a uterus) that, after estrogen and progesterone injections, displayed mating behavior. From this, he concludes:

> If the diagnosis of congenital absence is correct, it follows that behavioral mechanisms in the case of pigeons and the one rat attained a functional condition in the total absence of sex hormones.[34]

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[32] Frank Beach, whose research is explored later, writes:

> Although authorities generally agree that one major function of the hormones in the adult animal is to increase the stimulability of the behavioral mechanisms, there are some writers who believe that the hormones have another very important responsibility, namely the control or direction of the developmental organization of the mechanisms.

Beach cites Stone as an example of the latter. Beach, F. A. (1949). Hormones and Behavior: A Survey of Interrelationships Between Endocrine Secretions and Patterns of Overt Response. New York, Paul B. Hoeber, Inc. Medical Book Department of Harper & Brothers.

[33] Riddle, O. (1927). "The Quantitative Theory of Sex." Science **66**(1703): 169 - 170.

[34] Beach, F. A. (1949). Hormones and Behavior: A Survey of Interrelationships Between Endocrine Secretions and Patterns of Overt Response. New York, Paul B. Hoeber, Inc. Medical Book Department of Harper & Brothers.

That is, while hormones are necessary for the manifestation of mating behavior, they are not necessary for the functional organization of that behavior. In contrast to Stone's claim, hormones do not direct the organization of sexual mechanisms; they play only a stimulatory role. Something else creates the template upon which hormones can act. (As we shall see, this "something else" was thought to be genes or learning.)[35]

A second line of evidence that post-natal gonadal hormones are not essential to the organization of sexual behavior mechanisms comes from the observations of Boling, Blandau, Wilson and Young (1939) of newborn guinea pigs. They noticed that, in response to tactile stimulation, pups of both sexes would execute feminine mating behaviors for a few hours after birth. Presumably:

> These reactions, which are characteristic of the adult female in heat, appear in newborn infants under the influence of maternal hormones; at any rate the observations establish the fact that in this species the essential neuromuscular mechanisms for the feminine mating response are fully organized prepartum.[36]

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[35] William Perloff, studing humans with endocrine abnormalities, concurs:

> From these observations it would appear that in the human, libido and potency may be present and even normal though the gonadal hormones are diminished or absent. This would imply that these hormones are not necessarily essential to the libidinous urge, although, as will be shown later, they may indirectly influence the libido by affecting a common end organ.

Perloff, W. H. (1949). "Role of Hormones in Human Sexuality." Psychosomatic Medicine: Experimental and Clinical Studies **11**(3): 133 - 139.

[36] Beach, F. A. (1949). Hormones and Behavior: A Survey of Interrelationships Between Endocrine Secretions and Patterns of Overt Response. New York, Paul B. Hoeber, Inc. Medical Book Department of Harper & Brothers.

Finally, Beach found that male rats gonadectomized at different periods of development (from zero to 350 days after birth) displayed similar mating behavior after daily injections of androgen. Specifically, males castrated at birth showed just as much excitement and mounted receptive females just as often as males that had been castrated as adults. Beach takes this to:

> Indicate that postnatally secreted testis hormone is not essential to the organization of the neuromuscular mechanisms for mating in the rat. (However, penis growth was markedly inhibited by loss of the testes at birth and consequently animals so treated rarely achieved intromission and with one exception never ejaculated.)[37]

From these three lines of evidence, Beach comes to a number of conclusions regarding the organization of sexual behavior. First, that gonads are not necessary for this process. Second, that hormones are not the causal agents behind organization. Finally, that the neuromuscular elements necessary for hormonally conditioned behavior patterns (such as courtship, mating and parenting) "are fully organized and ready to function relatively early in life, well in advance of the time that they will be normally activated."[38] For Beach, the organization is due to early socialization.

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[37] Ibid.

[38] Ibid. Beach continues,

> They may be completely developed at birth or attain this condition at some time thereafter, but their organization is complete prior to the time that the hormones which will sensitize them to stimulation are secreted in sufficient quantities to become effective.

Beach, F. A. (1949). Hormones and Behavior: A Survey of Interrelationships Between Endocrine Secretions and Patterns of Overt Response. New York, Paul B. Hoeber, Inc. Medical Book Department of Harper & Brothers.

Specifically, while the neuromuscular elements may be fully organized, Beach also claims that there is a psychological component to the organization process. (This hypothesis is discussed in the next section.) It should be noted that this separation of mating into two components, organization and activation, not only directed Beach's research, but set the conceptual framework for the later development of the field.

V. Conclusion

The development of the field of endocrinology shifted the focus of research from external to internal factors. From an initial, vague hypothesis about the existence and function of hormones, scientists set about determining the nature and number of these hormones, with the goal of moving from a (merely) descriptive to an explanatory model. The goal of developing such a model was to explain not just physiological development, but the etiology of sexual behavior.

Explanatory models in the history of endocrinology are choosen through crucial resolutions, the topic of the next chapter.

Chapter 2

Crucial Resolutions in Endocrinology

I. Introduction

While the progress of science has been described by some as proceeding by a series of "crucial experiments," I claim that a critical factor in the development of many scientific fields is that of what I call "crucial resolutions" of outstanding anomalies. In contrast to crucial experiments, crucial resolutions are proposed to solve persistent anomalies or conflicting theoretical positions – often in advance of experimental confirmation. In what follows, I illustrate this point using a specific example from the history of endocrinology.

For a resolution to count as crucial it requires, at minimum, a collection of anomalies (perhaps just one) which arise in a situation of competition between "elaborated hypotheses"[39] (as opposed to initial postulations). Crucial resolutions are not just inferences to unobservables; when scientists initially propose them, they seem to resolve the anomalies which are regarded ex post facto as decisive, as in providing adequate grounds for deciding in favor of one or another of the elaborated hypotheses. It is the decision between elaborated hypotheses, based on their relative merits with respect to explaining anomalies, that is a crucial resolution. When scientists determine one specific problem (or set of problems) to be crucial they make a choice about what problems are the most important in a particular discipline at a particular time. As a result, the elaborated hypotheses offered to solve these problems serve as a construing of the

[39] Elaborated hypotheses (term due to Dennis Des Chene) have three characteristics: they have convincing, but not definitive, empirical support; as such, they explain part of, but not all, of a particular problem; two or more elaborated hypotheses are offered as solutions to unresolved problems. An example is hypotheses concerning the origin of life on earth. Abiogenesis is the hypothesis life originated from chemical processes on earth, panspermia the hypothesis that life came to earth from somewhere else. Both are supported by convincing, but not conclusive, evidence.

state of a field. Finally, the choice between elaborated hypotheses (the crucial resolution) shapes the subsequent development of a discipline.

While a crucial resolution directs the path a field will take, these resolutions are not "revolutions," in the Kuhnian sense. As the following chapters demonstrate, crucial resolutions decide between already existing elaborated hypotheses, as opposed to radically changing a world view.

Endocrinologists are very clear that "crucial resolutions" supply answers to previously unresolved issues, as well as providing direction for new research programs. There have been a number of such resolutions in the development of the field; in the following two chapters, I focus on one particular resolution that occurred in the late 1930's to the early 1940's. The issue in this case was whether in feminine embryonic development the mere *absence* of male hormones suffices, or if specifically *female* hormones are required. As intimated by the previous discussion of "inductive stuffs," this reflects the initially gendered framework vis a vis gonadal secretions.

In this period, some researchers postulated both a male hormone and a female hormone that guided the impetus for male and female development, respectively. This position is referred to in the literature as "di-hormonic." Other researchers hypothesized that only one substance was needed for male development; female embryonic development proceeded in the absence of hormonal stimulus. Importantly for my argument, researchers decided in favor of one or the other view based their capacity to explain certain anomalous phenomena. The view that has the greatest explanatory scope, that explains the most anomalous phenomena, resolves the "crucial" problems in a "crucial" fashion.

Two points of philosophical interest fall out of history of this debate. First, and most generally, not all successful explanations of persistent anomalies are taken to be crucial resolutions. I address reasons for this towards the end of this chapter. Second, experiments designed to provide empirical support for a particular resolution often yield ambiguous results. Yet the experiments often are interpreted by a large part of the scientific community as providing solid confirmation. I also address this incongruity.

These two points are historically related, but conceptually distinct. In what follows, I present a history of endocrinology (focused on this specific question) in order to demonstrate that:

> (1) Crucial resolutions occur.
> (2) They are often formulated in response to initial, anomalous test results, but in advance of convincing empirical experiments, and thus are not equivalent to crucial experiments.
> (3) They inspire research programs to determine the precise mechanisms in the causal chain initiated by the postulated substances.
> (4) The crucial experiments generated by the research programs are often interpreted as supporting the crucial resolutions more strongly than the evidence allows.

In what follows, I present arguments for both views concerning hormones and physical development, as well as some explanatory problems they face. I then discuss the crucial resolution of this debate, and the reaction of the scientific community. My main point is that crucial resolutions are postulated to resolve conceptual problems, and are so postulated in advance of unambiguously confirming empirical evidence. In addition, crucial resolutions are accepted in spite of ambiguous empirical evidence.

II. One Hormone or Two?

Researchers in the 1930's discovered that injecting androgens into the developing fetuses of female rats and rabbits masculinized both their internal and external genitalia.[40] This started a debate about the organizing potential of androgens and estrogens *in utero*. Scientists knew that androgens could masculinize female embryos, but could estrogens feminize male embryos? In other words, what role, if any, do the estrogens play in physical sexual development?

Advocates of the di-hormonic theory held that both androgens and estrogens are actively involved in sexual differentiation. Wiesner presents the di-hormonic view as follows:

> It is believed that the primordial of the genital organs are forced into male differentiation if and when the gonad develops into a testis and secretes male hormone; they become female if the gonad anlage assumes female type and produces a female hormone.[41]

A belief that echoes the initial presumption of inducing "material substances" (e.g., Conklin, 1933).

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[40] E.g. Moore, C., and Dorothy Price (1930). "The Question of Sex Hormone Antagonism." Proccedings of the Society for Experimental Biology and Medicine **28**: 38 - 40. and Dantchakoff, V. (1937). "Embryogenie Experimentale." Compte Rendue de Seances de L'academie des Sciences: 195 - 200.

[41] Wiesner, B. P. (1934). "The Post-Natal Development of the Genital Organs in the Albino Rat." The Journal of Obstetrics and Gynaecology of the British Empire **61**: 867 - 922.

One proponent of this view was R. R. Greene, who injected high levels of estrogens and androgens into pregnant rats in order to determine the effects on the offspring. He found, contrary to the mono-hormonic theory, that estrogens have a profound effect on embryonic development. Genetic males born from treated mothers exhibited a marked inhibition of the internal genitalia. In one experiment, fourteen out of nineteen treated males had visible nipples, which were not normally seen in the male rats of the colony used. Furthermore, in six of the animals, "there was a vagina which was comparable in development to that found in a normal new-born female."[42]

These results, combined with his later studies of the effects of androgens on females, led Greene to conclude that "the available facts concerning mammalian development are more compatible with the di-hormonic theory."[43] In addition, the di-hormonic theory was more compatible with otherwise inexplicable facts. Researchers at this time (and far into the future) did not know why the Müllerian ducts (which, if not inhibited, develop into the fallopian tubes, uterus, cervix and inner vagina) disintegrated in genetic males with typical androgen exposure. The di-hormonic theory could give a putative answer to this question: female hormones were required to stimulate them. Without this stimulation, they disintegrated.

While the results of Greene provide convincing support for the di-hormonic theory, they are not definitive. As will be discussed, other experimental results appeared

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[42] Greene, R. R., Burrill, M. W., and Ivy, A. C. (1938). "Experimental Intersexuality: The Production of Feminized Male Rats by Antenatal Treatment with Estrogen." Science **88**(2275): 130 - 131.

[43] Greene, R. R., Burrill, M. W. and Ivy, A. C. (1939). "Experimental Intersexuality: The Effect of Antenatal Androgens on Sexual Development of Female Rats." The American Journal of Anatomy **65**: 416 - 455.

to undermine the theory. In addition, while the di-hormonic theory could offer a solution to the long-standing question about Müllerian duct disintegration, it could not explain another persistent anomaly, what I call the "wrong medium" problem.

In contrast to the di-hormonic view, the "mono-hormonic" theory "recognizes the absolute dominance of the male hormone in developmental processes and it describes the conditions under which female differentiation may occur in *the absence of any*, rather than in the presence of a *specific, sex hormone*."[44] In short, only the male hormone is active in sexual differentiation in mammals; females develop as a result of the lack of androgens, as a "default," or "neutral" developmental path.

In defense of the mono-hormonic theory, its advocates pointed out that earlier results had shown that androgen exposure masculinizes female fetuses. In itself, these experimental results do not conflict with the di-hormonic theory. However, those arguing in favor of the mono-hormonic theory make the additional claim that female hormones do not feminize male fetuses – implying that female hormones are inactive during embryonic development.

Wiesner's studies of castrated female rats support this latter claim. He discovered that, macroscopically, there was no difference between controls and gonadectomized females in 23 out of 29 cases. Even though internal measurements of the uteri revealed underdevelopment in five of these cases,[45] Wiesner concludes:

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[44] Wiesner, B. P. (1935). "The Post-Natal Development of the Genital Organs in the Albino Rat." The Journal of Obstetrics and Gynaecology of the British Empire **62**: 8 - 75.

[45] Wiesner, from his experiments, notes that:

> It appears that the uterus of the oopherectomized [female gonadectomized] animals is, in most instances, of about the same diameter as that of the control females . . . Deviations in either direction appear, but are, as a rule, of insignificant magnitude.

> Prepubertal development of the genital organs thus appears to be independent of ovarian hormones. . . This conclusion appears not to be invalidated by the partial inhibition of development that occurred in five cases.[46]

Thus, even though the empirical results were ambiguous, Wiesner considers the mono-hormonic theory to be a better explanation of embryonic development. I suspect that this is not (merely) a case of dismissing a small number of unexpected results as "noise," but an attempt to address the general finding that male hormones induced masculinization of fetuses, while female hormones (for the most part) did not. In short, there appeared to be an asymmetry in their developmental effects.

As a result of this apparent asymmetry, one advocate of the mono-hormonic theory, R. K. Burns, writes:

> One is impressed with the apparent unimportance of female hormone contrasted with the ability of male hormone to remodel female external parts. We have long been puzzled by the fact that in the fetus of mammals male development pursues its normal course untroubled by large quantities of female hormone in the placenta and amniotic fluid. *We should seriously consider the possibility that in mammals a mon-hormonic system of control largely prevails*, perhaps especially evolved as an adaptation to intrauterine development.[47] [My emphasis]

Wiesner, B. P. (1934). "The Post-Natal Development of the Genital Organs in the Albino Rat." The Journal of Obstetrics and Gynaecology of the British Empire **61**: 867 - 922.

[46] Ibid.

[47] Burns, R. K. (1938). "Hormonal Control of Sexual Differentiation." The American Naturalist **72**(740): 207 - 227.

Here, Burns is referring to the "wrong medium" problem: how can typical male differentiation occurs within a female medium? Specifically, pregnant mammals produce high levels of estrogens that can traverse the placenta and reach the fetus. From this advocates of the mono-hormonic theory conclude that, if estrogens had any effect on sexual differentiation, all genetic male embryos would be feminized.

Wiesner, for instance, offers this argument. In addition, he claims that the mono-hormonic theory is to be preferred because it explains a wide variety of developmental etiologies in a more simple fashion:

> When discussing the dihormonic theory attention was directed, in the first instance, to the limitations of its experimental basis. But the main objections which were brought forward against the dihormonic theory, and which caused one to reject it, were derived from its failure to explain adequately and with reasonable economy of hypothesis, certain experimental facts, observations relating to normal embryonic development and, last but not least, teratological cases.[48]

"Economy of hypothesis" is with respect to explaining both (1) the typical male development, even after embryonic exposure to female hormones, and (2) ovarian activity over the course of normal female development. ("Tetratological" refers to cases of intersexuality.) We should note that the "economy" is not with respect to entities (that is, the number of hormones) but with respect to causal roles (the number of agents needed to instigate both typical and atypical outcomes). As I discuss in chapter 7, this appeal to economy of hypothesis echoes the Kitcherian ideal of simplicity

[48] Wiesner, B. P. (1935). "The Post-Natal Development of the Genital Organs in the Albino Rat." The Journal of Obstetrics and Gynaecology of the British Empire **62**: 8 - 75.

The economy of hypothesis that explains the former problem (that of the wrong medium) by postulating that female hormones – both embryonic and maternal – have no effect on the development of the fetus. In other words, female hormones don't act as a causal agent during embryonic development.

The latter involves a second unresolved problem: that of timing. Because female puberty is defined in terms of "sex cycles" (estrus in lab animals), and these cycles are absent before puberty, it was generally assumed that ovarian function does not begin until puberty. Combining this with the di-hormonic theory of embryonic development, Wiesner points out that:

> Thus some authorities are inclined to regard puberty as marking the inception of gonadic function in the female while, on the other hand, it is assumed with almost equal assurance that female differentiation proceeds under the influence of, and is dependent on, secretions of the ovary. It is astonishing that this contradiction could not only persist in the literature without being subjected to experimental examination, but could be expressed by one and the same author.[49]

In other words, some scientists advocating the di-hormonic theory had put forth the inconsistent claims that female embryonic development requires hormones secreted by the ovary *and* the claim that female gonads do not become active until puberty.[50]

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[49] Wiesner, B. P. (1934). "The Post-Natal Development of the Genital Organs in the Albino Rat." The Journal of Obstetrics and Gynaecology of the British Empire **61**: 867 - 922. Perhaps for reasons of professional diplomacy, Wiesner does not name specific authors.

[50] Contemporary endocrinology supports a more subtle version of this view: the gonads secrete "sex" hormones (of both types) during embryonic development, then they become dormant, and become active again during puberty. This theory of etiological development resolves the contradiction mentioned by Wiesner.

Wiesner offers the mono-hormonic theory as a means of resolving this contradiction (as well as the problem of the wrong medium):

> It will be seen that the occurrence of male differentiation in the female medium can hardly, if at all, be reconciled with the dihormonic theories; but it does not present any difficulty to the monhormonic theory. The latter submits that ovarian hormones are neither necessary for female differentiation nor capable of accelerating it. It was concluded that female hormone must meet with a differentiated female system in order to exert any noticeable effects, but cannot evoke the system upon which it is to act. If feminization is not an effect of female hormone but a condition for the activity of the hormone, then it is clear why a male embryo (in which female differentiation has not occurred) does not react to female hormone.[51]

Given the presence of female hormones in the pregnant female, the di-hormonic theory cannot explain why this does not interfere with male development. However, the mono-hormonic theory can provide an explanation for this - female hormones are not necessary for female embryonic development. As such, female hormones are necessary only for the activation of puberty. Ovarian hormones act only upon a differentiated female system, but do not stimulate this system to differentiate *in utero*. This solves the initial question of why female hormones do not interfere with typical male development.[52]

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[51] Wiesner, B. P. (1935). "The Post-Natal Development of the Genital Organs in the Albino Rat." The Journal of Obstetrics and Gynaecology of the British Empire **62**: 8 - 75.

[52] Wiesner concludes that "the physiology of the sex cycle thus can hardly be identical with the physiology of the prepuberium." Wiesner, B. P. (1934). "The Post-Natal Development of the Genital Organs in the Albino Rat." The Journal of Obstetrics and Gynaecology of the British Empire **61**: 867 - 922.

It should be noted that Wiesner adopts the mono-hormonic hypothesis for reasons of *simplicity*. Specifically, the etiological development of the pre-pubertal pubertal female is solely the result of genetic constitution, not hormonal influence:

> For reasons of simplicity, in view of the general physiological considerations, and in accordance with the principal assumption of this discussion, it may be assumed, therefore, that the differentiation in female direction of the indifferent genital anlagen occurs independently of ovarian hormones. In other words, it may be concluded that the genetic constitution of the somatic cells of the zygotic female is sufficient to invoke their female differentiation.[53]

In addition to the appeal of explanatory simplicity that embodies Kitcher's ideal of unification, this history of scientific investigation also accords beautifully with Craver's discussion of the distinction between "how possibly" and "how actually" explanatory models. Both the mono- and di-hormonic hypotheses fit the data, although with notable incongruities; they are, at this point in time, "how possibly" models.

However, the resolution of the contradiction mentioned above, as well as that of the "wrong medium" problem, were not regarded as "crucial." Because of conflicting and ambiguous results (such as those from Greene), laboratory tests do not provide incontrovertible proof of the mono-hormonic theory. But the mono-hormonic theory *could* provide a theoretical resolution where the di-hormonic theory could not: a resolution of the "freemartin problem."

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[53] Wiesner, B. P. (1935). "The Post-Natal Development of the Genital Organs in the Albino Rat." The Journal of Obstetrics and Gynaecology of the British Empire **62**: 8 - 75.

III. The Freemartin Problem and Frank Lillie's Resolution

Freemartins were an etiological mystery as well as an economic problem (and are to this day).[54] Freemartins are the female half of male-female bovine twins, exhibiting pseudo-hermaphroditism in the form of masculinized internal genitalia and behavior. Specifically, freemartins display markedly inhibited Müllerian ducts, and moderately masculinized Wolffian ducts. One of the key facts that distinguish freemartins from other pseudo-hermaphrodites is that the internal, but not the external, genitalia are profoundly masculinized.

However, the male halves display no pseudo-hermaphroditism. The cause of this asymmetry was a long-standing problem in the field of endocrinology. Frank Lillie, the subject of this section, is famous for the initial resolution of the freemartin problem.

When endocrinologists refer to the resolution of the "freemartin problem," I have discovered that they can refer to one of two related, but conceptually distinct, resolutions. In the history of endocrinology, there have been two "resolutions" to this problem – the first proposed by Frank Lillie, who deduced the general mechanisms behind the freemartin, the second proposed in terms of the mono-versus di-hormonic debate. The latter of these resolutions is crucial, the former is not. The important philosophical point, for my purposes, is not there were two resolutions, but that the first was radically re-interpreted in light of the latter. In other words, Lillie's resolution became crucial after the fact.

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[54] "In a dairy production system, freemartins are of little economic value because their ability to conceive and subsequently lactate is impaired, unless a market for dairy beef exists." Padula, M. (2005). "The Freemartin Syndrome: An Update." Animal Reproduction Science **87**: 93 - 109.

Lillie's initial resolution had several important impacts on the field of endocrinology: it crystallized a method of investigation; shifted the emphasis of developmental etiology from genetic to hormonal factors; and provided a crucial platform for the triumph of the mono-hormonic theory of embryonic sexual differentiation. [55]

Lillie came to the realization that studying deviations from the typical developmental process could shed light on *both* deviant and typical outcomes. In other words, studying the "exceptions" to the (observed) rules could illuminate the (mechanisms of) rules themselves. According to Blanche Capel and Doug Coveney:

> This monumental contribution re-focused the field of mammalian reproduction, laying the framework for advances in reproductive endocrinology and sex differentiation in the 20th and 21st centuries.[56]

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[55] Witschi notes:

> A closer analysis of the inductor activity indicates, furthermore, that the visible morphological differentiations are evoked by special chemical substances which are produced and released by the inductors. This assumption was probably first suggested and supported by F. R. Lillie in his classical studies on the cattle free-martins. The now well equally established fact that in primates a similar exchange of blood between male and female embryos does not interfere with normal sex development cannot reduce the importance of the free-martin case; though it proves that the mechanism of induction deserves a more detailed investigation.

Witschi, E. (1937). "Stimulative and Inhibitive Induction in the Development of Primary and Secondary Sex Characters." Proccedings of the National Academy of Sciences of the United States of America **23**(1): 35 - 39.

[56] Capel, B., and Coveney, Doug (2004). "Frank Lillie's Freemartin: Illuminating the Pathway to 21st Century Reproductive Endocrinology." Journal of Experimental Zoology **301A**: 853 - 856.

Lillie's basic methodology remains to this day the core of developmental endocrinological research: induce[57] and investigate deviations from the norm in order to understand the mechanisms of both typical and atypical development.

Before Lillie's resolution, many biologists (including, initially, Lillie himself) believed the freemartin to be an insufficiently masculinized genetic male. In terms of causation, this meant that the genes determining sex, rather than hormones, were the primary agents of sexual differentiation.[58] However, subsequent examinations of male/freemartin fetuses revealed them to be dizygotic, rather than monozygotic, twins. According to Capel and Coveny:

> Because internal organs are phenotypically male in freemartins, most breeders and other biologists believed that the freemartin must be an insufficiently masculinized genetic male. . . . Lillie questioned this interpretation on the grounds that it did not explain why the occurrence of freemartins was limited to cattle while other animals gave rise to twins of normal sexual phenotypes.[59]

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[57] Importantly, Lillie did *not* induce freemartins – he examined those post-natal specimens brought to his attention, or embryos from slaughtered cows. Due to the lack of knowledge about the causes of the freemartin phenotype (which is distinct from other sorts of female pseudo-hermaphroditism), endocrinologists have not been able to reproduce the freemartin effect under laboratory conditions until approximately 20 years ago. With other animals, however, advances in hormone isolation allowed for inducement.

[58] For instance:

> Hart argued that the freemartin phenotype formed as a consequence of monozygotic twinning in a male embryo. At the time of twinning, the gonad-forming region was segregated to only one twin which became the male while the other twin became the freemartin.

Freeman, G. (2007). "Explaining the Freemartin: Tandler and Keller vs. Lillie and the Question of Priority." Journal of Experimental Zoology **308B**: 105 - 112.

[59] Capel, B., and Coveney, Doug (2004). "Frank Lillie's Freemartin: Illuminating the Pathway to 21st Century Reproductive Endocrinology." Ibid. **301A**: 853 - 856.

For Lillie, the freemartin problem became not just a question of its developmental etiology, but also why the condition was (apparently) exclusive to cattle. He believed that answering the second question would answer the first.

Lillie concluded that, because the placentas of bovine twins can fuse in utero, the developing testis of the male produces a substance that influences the development of the female, thus producing a freemartin. Crucially for my argument, Lillie did not describe the substance as an androgen, but simply as a "male factor." The crucial resolution (to be discussed later) made the assumption that freemartins were the result of androgen exposure. While freemartins are the result of a "male factor," the primary factor is not an androgen, but the Müllerian inhibiting substance:

> In the case of a heterosexual twin pregnancy the female foetus exposed to AMG [anti-Müllerian gonadotropin] (produced by the testes of its male twin and circulating through placental vascular anastomoses), shows ovarian stunting and develops various degrees of masculinization, including uterine and vaginal hypoplasia, accompanied by occasional presences of male genital tract derivatives.[60]

Lillie correctly concluded that freemartins occur in cases of dizygotic twinning where one twin is genetically male and the other genetically female. This fundamental shift in view had profound implications for sexual development. First, it implied that the

[60] Rota, A., et. al. (2002). "Age Dependent Changes in Plasma Anti-Mullerian Hormone Concentrations in the Bovine Male, Female, and Freemartin from Birth to Puberty: Relationship Between Testosterone Production and Influence on Sex Differentiation." General and Comparative Endocrinology **129**: 39 - 44.

internal reproductive organs may not always be the most reliable measure of genetic sex. Second, it indicated that the freemartin was not the result of sub-male development, but rather the result of active disruptive influences of the male twin on female development.[61]

Lillie proposed that sex characteristics in mammals are controlled by (1) a primary zygotic determinant (which we now refer to as "genetic sex") and (2) secondary internal secretions that play specific roles in the differentiation of certain sex characteristics.[62] Lillie also pointed out "that the female zygote must contain factors for both sexes; the primary determination of the female sex must therefore be due to the dominance of female factors over the male."[63]

Lillie's studies were published at the time when the mono- versus di-hormonic debate still raged. It is interesting to note that Lillie phrases his conclusions in such a way that could be read to support either of the competing theories.

On the face of it, it is not clear whether the dominant "female factors" are those of genetic sex, female hormones, or both. To account for the one-way effect of sex reversal in freemartins (i.e., why male embryos subvert the development of their female co-twin, but females do not affect their anastomosed male partner), Lillie hypothesized a combination of both kinds of factors. He pointed to evidence for the earlier appearance of steroidogenic cells in males, and concluded that differentiation of males occurs early

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[61] Capel, B., and Coveney, Doug (2004). "Frank Lillie's Freemartin: Illuminating the Pathway to 21st Century Reproductive Endocrinology." Journal of Experimental Zoology **301A**: 853 - 856.

[62] Hartman writes: "The principle of hormone influence in fetal life, first demonstrated by Lillie, constitutes the most important contribution to the subject as yet made." Hartman, C. (1920). "The Free-Martin and its Reciprocal: Opossum, Man, Dog." Science **52**(1350): 469 - 471.

[63] Quoted in Capel, B., and Coveney, Doug (2004). "Frank Lillie's Freemartin: Illuminating the Pathway to 21st Century Reproductive Endocrinology." Journal of Experimental Zoology **301A**: 853 - 856.

enough to influence female development whereas development of females occurs too late to affect development of the male co-twin. When it comes to bovine twins:

> If both are males or both are females no harm results from this; but *if one is male and the other female, the reproductive system of the female is largely suppressed, and certain male organs even develop in the female. This is unquestionably to be interpreted as a case of hormone action.* It is not yet determined whether the invariable result of sterilization of the female at the expense of the male is due to more precocious development of the male hormones, or to a certain natural dominance of male over female hormones.[64] [Original emphasis]

In other words, Lillie did not interpret his results as providing a resolution to the mono- versus di-hormonic debate.

IV. Resolution of the Freemartin Problem as Crucial

In spite of Lillie's agnosticism, later scientists interpreted Lillie's findings as conclusive proof of the mono-hormonic theory. One reason for this was that the mono-hormonic theory could explain the freemartin problem in a much more simple and straight-forward fashion than the di-hormonic theory.

According to the di-hormonic theory, the hormones of the female twin should effect the development of the male twin, not just the female. Both male and female embryos sharing the same womb should become pseudo-hermaphrodites (even though

[64] Lillie, F. (1916). "The Theory of the Free-Martin." Science **43**(1113): 611 - 613.

this demonstrably is not the case in primates). Wiesner points out that di-hormonic theory cannot:

> [E]xplain why the presence of female hormone in the amniotic fluid of certain species does not affect male differentiation of the embryo. It has been suggested, in the resulting embarrassment, that the female hormone (oestrin) present in the amniotic fluid is not identical with the embryonic ovarian hormone which directs female differentiation; it still remains to be explained why the hypothetical embryonic female hormone of the free-martin fails to disturb the differentiation of the male twin of the free-martin.[65]

Thus the problem: the di-hormonic assumption that the female hormone is "active" during embryonic development cannot explain why only the female bovine twin displays pseudohermaphroditism. To resolve this problem, Wiesner and others advocate the mono-hormonic theory: only the male hormone is active during embryonic development, thus affecting both male and female fetuses alike.[66] On the face of it, this is an entirely plausible interpretation. Unfortunately for mono-hormonic advocates, attempts to replicate the freemartin effect in laboratory animals were completely unsuccessful. Specifically, exposing female embryos to testosterone, while

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[65] Wiesner, B. P. (1934). "The Post-Natal Development of the Genital Organs in the Albino Rat." The Journal of Obstetrics and Gynaecology of the British Empire **61**: 867 - 922.

[66] Capel writes:

> Based on these observations, Lillie developed a hormone theory of the freemartin effect, in which he proposed that partial male development is imposed on the female twin by circulating sex hormones produced by her male co-twin.

Capel, B., and Coveney, Doug (2004). "Frank Lillie's Freemartin: Illuminating the Pathway to 21st Century Reproductive Endocrinology." Journal of Experimental Zoology **301A**: 853 - 856.

masculinizing the external genitalia, did not masculinize the internal genitalia. This discrepancy is, in part, the motivation for Jost's work, discussed in the following chapter.[67]

This resolution, unlike those of the "timing" and "wrong medium" is crucial. In what follows, I present some initial reasons why the resolution of the freemartin problem was regarded as crucial, while those of timing and media were not.

As I mentioned at the beginning of this chapter, crucial resolutions are often presented in advance of unequivocal experimental confirmation. Although the mono-hormonic theory was held to have resolved questions of timing and medium, the experimental data were in fact ambiguous. In contrast to those earlier issues, the resolution of the freemartin problem avoided troublesome empirical results of the sort discovered by Greene and Wiesner.

Because cattle are not often used as laboratory animals, the freemartin data took on the character of a thought experiment. Very few endocrinological experiments were performed on large mammals – including cattle – on account of financial, spatial and temporal issues.[68] Lillie was able to complete his studies only because he owned a large cattle farm and had developed good connections with some Chicago stockyards. Because

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[67] As Rota points out:

> Jost (1953) was the first to suspect that testicular tissue not only produced testosterone, the chemical responsible for the development of male external genitalia in rabbit fetuses, but also produced a substance that induced regression of the Müllerian ducts.

Rota, A., et. al. (2002). "Age Dependent Changes in Plasma Anti-Mullerian Hormone Concentrations in the Bovine Male, Female, and Freemartin from Birth to Puberty: Relationship Between Testosterone Production and Influence on Sex Differentiation." General and Comparative Endocrinology **129**: 39 - 44.

[68] Interestingly, after Lillie offered his initial resolution, very little work was done on freemartins. Contemporary research is published primarily in veterinary journals.

of its resemblance to a thought experiment, Lillie's work could be idealized by later commentators as containing no empirical ambiguities.

The resolution of the freemartin problem also solved those of timing and media. This specific resolution shares many similarities with another: Einstein's resolution of the conflict between the constant speed of light and the addition of velocities. His theory of special relativity depended heavily upon thought experiment; it resolved several outstanding problems and was presented (and largely accepted) in advance of experimental confirmation. Much like the initial resolution presented by Lillie, the famous Michelson-Moreley experiments were reinterpreted in light of special relativity.

The answer to the freemartin problem, moreover, resulted in:

> [T]he end of a problem of long standing and the beginning of a period of experiments on the mechanisms of sex differentiation, differing widely in method but having in common the theoretical conception developed for the freemartin – that sex-specific hormones are produced, circulate with the blood and act upon the appropriate embryonic structures during the plastic stages of development.[69]

In other words, the resolution of the freemartin problem, like the adoption of special relativity, initiated a new research program devoted to understanding the mechanisms behind androgen-stimulated embryonic development.

V. Conclusion

[69] Burns, R. K. (1938). "Hormonal Control of Sexual Differentiation." The American Naturalist **72**(740): 207 - 227.

The scientific community of endocrinologists during this time period, in the main, accepted the resolution of the freemartin problem as crucial. This resolution is crucial because it solved not just the freemartin problem, but also was perceived as conclusive evidence for one of two elaborated hypotheses. In spite of its "thought-experiment" like character, this resolution not only inspired a general research program, but also influenced how scientists interpreted the results of this program. (I address this in the following chapter.)

More generally, crucial resolutions are sometimes formulated in response to initial, anomalous test results, but in advance of convincing empirical experiments, and thus are more like thought experiments than those performed in the laboratory. Which solutions to problems (and hence which problems) turn out to be crucial is not determined solely by the formal features of the hypothesis or its content. Instead, crucialness is a construction placed upon the "problem-solution" field at a particular point of time: those problems deemed the most important, and the elaborated hypotheses proposed to solve them, set the stage for crucial resolutions.

That a hypothesis offers a crucial resolution sometimes leads to an over-estimation of the evidence in its favor, as well as a simplification of the results. This can be seen in the scientific community's general interpretation of Lillie's initial resolution and, as discussed in the next chapter, the experimental results of Jost. Part of the reasons for this were the assumptions made about the nature of the competing hypotheses. A

more interesting part (for my purpose) is due to the importance of the resolution to the field of endocrinology in general.

These resolutions inspire research programs – in the case of endocrinology, a program to determine the precise mechanisms in the causal chain initiated by the postulated substances. Because of the tendency to give crucial resolutions more weight than the evidence merits, as well as the tendency to over-simplify the results, they can determine the course of a discipline and, as such, the actual body of knowledge. This is discussed more thoroughly in the following three chapters.

Chapter 3

The Logic of Discovery and Jost's Experimental Confirmation

I. Introduction

While it has been a standard view in philosophy of science that there can be no logic of discovery, I argue that the phenomenon of crucial resolutions demonstrates that there can be. Specifically, the formulation of elaborated hypotheses and the crucial resolutions that decide between them contitute a logic of discovery. This claim, on the

face of it, is ambiguous: for, as I argue, several discussions have equivocated on the term 'discovery,' and have been less than clear about what it means for discovery to have a 'logic.' In what follows, I aim to disambiguate these terms.

In his 1973 article, "Does Scientific Discovery Have a Logic,"[70] Herbert Simon argues that it does, albeit not in the narrow, Popperian sense.[71] Simon suggests that this disbelief in the possibility of a logic of discovery rests upon the assumption that any normative theory of discovery invokes the long-standing philosophical problem of induction: if the discovery of theories proceeds by induction upon (limited) data sets, how can we be sure that those inductions are correct? Because data sets outside the field of theoretical mathematics are, almost by definition, limited, any induction upon them must involve a "creative element."

Simon argues that this underlying problem of induction is a red herring. If one understands the process of discovery as that of interpreting, in a "parsimonious" fashion, sets of empirical data, and a normative theory of scientific discovery as a set of criteria for evaluating this discovery process, then, if we can give both a descriptive account of scientific discovery *and* a normative account of the process of discovery, we will have constructed a logic of discovery.

In what follows I detail how Simon's philosophical claims apply to the processes of discovery in the history of behavioral endocrinology. I claim that many, but not all, of Simon's arguments can be substantiated using examples within the history of the field.

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[70] Simon, H. (1973). "Does Scientific Discovery Have a Logic?" Philosophy of Science **40**(4): 471 - 480.

[71] While Reichenbach argues that the context of discovery is irrelevant to the context of justification, Popper makes the stronger claim that there can be no logic of justification.

In particular, I draw upon the mono- vs. di-hormonic debate discussed in the previous chapter although, as we shall see in later chapters, Simon's arguments can be instantiated with other examples. Both the elaborated hypotheses and the crucial resolutions that decide between them – the "discoveries" – contain a normative element. Their discovery is not capricious, but due to "good reasons."[72]

In addition, the logic of discovery influences the process of confirmation – and not merely by determining which problems to investigate. As I demonstrate with Jost's experimental confirmation of the mono-hormonic theory and, more importantly, the scientific community's reaction to it, many of the normative elements of discovery influence the process of confirmation. I discuss this in the final section of this chapter.

II. The Distinction

The distinction between the process of discovery (or invention) of scientific theories[73] and the practice of justifying those theories – as famously articulated by Karl Popper and Hans Reichenbach – implies that the process of discovery contains an irrational element. As such, there can be no normative theory of scientific discovery. While the claim that there can be no logic of discovery has been disputed by several

[72] Carl Kordig's phrase.

[73] Traditionally, this claim is phrased in terms of scientific laws. Because I discuss a particular sub-field of biology – a field that is traditionally more "messy" than that of, say, physics – I prefer to use the term 'theory' due to its less stringent implications.

philosophers,[74] few have undertaken detailed historical examinations to support this claim.

Popper, in his philosophical classic *The Logic of Scientific Discovery*, makes the strong claim that there is no logic to scientific discovery. He argues that:

> The initial stage, the act of conceiving or inventing a theory, seems to me neither to call for logical analysis nor be susceptible of it. The question how it happens when a new idea occurs to man – whether it is a musical theme, a dramatic conflict, or a scientific theory – may be of great interest to empirical psychology; but it is irrelevant to the logical analysis of scientific knowledge . . . my view of the matter, for what it is worth, is that there is no such thing as a logical method of having new ideas, or a logical reconstruction of this process. My view may be expressed by saying that every discovery contains an 'irrational element', or a 'creative intuition', in Bergson's sense.[75]

Popper's claim brings up two questions: (1) is it the case that every scientific discovery contains an irrational element? It is certainly the case that some do.[76] And (2): is it the case that the process of discovery is *solely* irrational? Interpreting Popper's claim

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[74] Including Kevin Kelly (1987), Andrew Lugg (1985), Nelson Hanson (1958), and, most famously, C. S. Pierce (1960).

[75] Popper, K. (1959). The Logic of Scientific Discovery. New York, Basic Books.

[76] Perhaps the most famous example of the "irrationality" of discovery is the case of Kekule's realization of the benzene ring structure through a dream. For a discussion of the potential rational aspects of Kekule's discovery, see. Koertge, N. (1982). "Explaining Scientific Discovery." PSA: Proceedings of the Biennial Meeting of the Philosophy of Science Association **1**: 14 - 28.

in light of the second question construes it in much broader terms than that of the first question: discovery takes on a "mystical"[77] quality.

Viewing Popper's claim in light of the first question brings up two additional questions. First, is it true? Are there cases of scientific discovery that do not contain irrational (or 'creative') elements? Second, if it is true, if there are irrational elements in every scientific discovery, does this automatically disbar it from logical analysis? As I argue later, the existence of irrational elements in hypothesis formation (in the case of behavioral endocrinology, cultural preconceptions about gender) does not preclude logical analysis. As such, Popper's strong claim is, strictly speaking, false.

But what about Reichenbach's weaker claim, that the logic of discovery is *irrelevant* to the logic of justification? Reichenbach introduces the terms 'context of discovery' and 'context of justification' to distinguish between the psychological origin of a claim and the epistemological evaluation of said claim. This distinction relies upon another: that of the distinction between psychology and epistemology.[78] If the initial

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[77] Simon's term. Several philosophers, while upholding the distinction, deny that the process of discovery is (in general) lacking of *all* rational elements. One such is Siegel, who points out that, for example:

> [I]t is perfectly compatible with Reichenbach's position that a scientist who keeps certain principles of justification in mind (say, that hypotheses must survive attempts at falsification; that they are likely to be "limiting cases" of previous theory; that they must not overlook crucial types of observational data; etc.) will be aided, by doing so, in the attempt at discovery.

Siegel, H. (1980). "Justification, Discovery, and the Naturalizing of Epistemology." Philosophy of Science **47**(2): 297 - 321.

[78] Harvey Siegel claims:

> These distinctions are closely related, in that the context of discovery is primarily concerned with the psychological origins of (scientific) ideas, while the context of justification is primarily concerned with the epistemological evaluation of such ideas. (Indeed, for Reichenbach, at any rate, the two distinctions may collapse into one.)

distinction between discovery and justification holds, and if there can be some sort of "logic" to the process of justification, is the same true for the process of discovery?

While some philosophers claim that the discovery/justification distinction, as initially introduced, contains an ambiguity in the notion of 'discovery,' I claim that there is also an ambiguity in the notion of justification. In particular, the acceptance of a hypothesis does not always coincide with its empirical justification; the acceptance of a resolution as crucial influences the interpretation of empirical attempts at confirmation. I address this later, in my discussion of Jost's experimental confirmation. But first, I present arguments in support of a logic of discovery.

III. Towards a Logic of Discovery

Several philosophers of science claim that there can be a logic of discovery. Historically, the arguments of C. S. Peirce have been the most influential. Peirce coined the term 'retroduction' as a label for the systematic processes leading to the discovery of scientific theories. Norwood Hanson adopts this term in his *Patterns of Discovery*, and gives as an example an account of the retroductive path, inferred from Tycho Brahe's data, that led Kepler to discovery the elliptical orbits of the planets.

Arguing against a "mystical" account of discovery, Hanson claims:

> H-D [hypothetical-deductive] accounts all agree that physical laws explain data, but they obscure the initial connexion between data and laws; indeed, they

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Ibid.

> suggest that the fundamental inference is from higher-order hypotheses to observation statements. This may be a way of setting out one's reasons for accepting a hypothesis after it is got, or for making a prediction, but it is not a way of setting out reasons for proposing or for trying an hypothesis in the first place. Yet the initial suggestion of an hypothesis is very often a reasonable affair. It is not so often affected by intuition, insight, hunches, or other imponderables as biographers or scientists suggest. Disciples of the H-D account often dismiss the dawning of an hypothesis as being of psychological interest only, or else claim it to be the province solely of genius and not of logic. They are wrong. If establishing an hypothesis through its predictions has a logic, so has the conceiving of an hypothesis.[79]

Hanson describes Kepler's retroductive thought process as struggling with Tycho's observational data of the orbit of Mars until he perceived a pattern in the phenomena: that the surprising data could be explained easily were the orbit an ellipse. Unlike proponents of the H-D view, Hanson interprets Kepler to have based his retroductive inference on the fact that there is a certain pattern within Tycho's data: "Perceiving the pattern in the phenomena is central to their being 'explicable as a matter of course.'"[80] As a result, Kepler's perception managed to pull together the "enormous heap of calculations, velocities, positions and distances which had set [him] his problem . . . into a geometrically intelligible pattern."[81]

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[79] Hanson, N. (1958). Patterns of Discovery. Cambridge, Cambridge University Press.

[80] Ibid.

[81] Ibid. After a careful reconstruction of Kepler's thought patterns, Lugg concludes:

> By thinking his [Kepler's] thoughts after him, we can follow him through the various stages of his inquiry and conclude – as Hanson does at the end of his description of the discovery – that he never projected explanations capriciously but always had good

But this intelligible pattern involves more than (merely) scrutinizing the data. Hanson claims that the conceiving of a hypothesis can appeal to the virtues of "explanatory fertility," "aesthetic elegance," "symmetry," as well as "simplicity."[82] These virtues, he claims, have a "rational function" in the process of formulating initial, plausible suggestions.

But herein lies one of the ambiguities alluded to earlier. On both Hanson's and Simon's account, "initial plausible suggestions" can mean either what I have been calling elaborated hypotheses, or it can refer to suggestions made during an earlier stage in the development of the field and, as such, can consist of plausible suggestions made initially (such as the suggestion that internal secretions play an important role in mammalian sexual development, as opposed to genetic factors *per se*.)

More abstractly, philosopher Carl Kordig, for instance, agrees with Hanson (and Simon) that there can be a logic of discovery, he claims that Hanson, in his discussion, equates "discovery" in general with initial plausibility.[83] This reflects an underlying ambiguity in philosophical discussions of discovery: the failure to distinguish between initial suggestions and *plausible* initial suggestions. To remedy this, Kordig proposes a tripartite distinction: initial thinking, plausibility, and acceptability.

> reasons for proposing the modification [of previous theories] he did. Kepler's investigations were certainly complicated and ingenious, but they were never recondite. Although his discovery was a work of great genius, we can in retrospect understand explain both his successes and failures. The brilliance of Kepler's achievement lay in the quality of his argument, not in its inscrutability.

Lugg, A. (1985). "The Process of Discovery." Philosophy of Science **52**(2): 207-220.

[82] Hanson, N. (1971). The Idea of a Logic of Discovery. What I do not Believe and Other Essays. T. a. Woolf. Dordrecht, D. Reidel.

[83] Kordig, C. (1978). "Discovery and Justification." Philosophy of Science **45**(1): 110 - 117.

Initial thinking – the imagining or guessing of hypotheses regardless of their plausibility – is, according to Kordig, a creative act. Here, Kordig concedes, relativists like Kuhn might be correct: cultural and psychological factors can influence initial thinking (as we have seen with the initial, gendered discussion of hormones). As such:

> The phrase "discovery of" often means "initial thought of." Here logic is not essential to discovery, as logical empiricists stress. Good reasons are not required to think, as all of us know at least sometimes. Initial thoughts – Kekule's dream of the Benzene ring, Poincare's intuition boarding a train, Ramanujan's divine illuminations, etc. – at times lack evidential reasons.[84]

Because of this lack of evidence, not every initial suggestion survives. Initial thought is prior to both plausibility and acceptance. Good reasons, essential to plausibility and justification, are not essential to initial suggestions. As such, initial thinking is logically distinct from both.

The second distinction Kordig makes, plausibility, is more difficult to disambiguate. Why might one initial thought be considered worthy of further pursuit, and not another? Kordig does not address this,[85] but discusses what makes one initial thought (hypothesis) more plausible than another. He points out that:

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[84] Ibid.

[85] Kordig's (brief) discussion of plausibility is ambiguous on this point. He writes:

> There are many ways to express this. Hypotheses are initially plausible prior to test. They are worthy of further consideration, though not yet acceptance. Consideration of one hypothesis rather than another is often reasonable. Good reasons may support an hypothesis' possible truth and promise.

Ibid.

> Scientists aware of two hypotheses, sometimes reasonably suggest that only one be considered further. One may be simpler than the other. Before test good reasons often support an hypothesis' being at least somewhat reasonable. After its initial psychological occurrence, an hypothesis may be elaborated, seriously proposed, deemed promising and plausible to explore.[86]

From Kordig's wording, it is not clear if initially plausible hypotheses, on his account, would count as elaborated hypotheses, with the choice between them a crucial resolution, or if the postulations take place earlier in the research process. For the sake of argument, I concentrate on the plausibility, or "reasonableness," of elaborated hypotheses.

We can see the virtues mentioned by Hanson at play in both the mono- and the di-hormonic theories of development. In terms of explanatory simplicity, the di-hormonic theory could not resolve the "wrong medium" or the "wrong timing" problem, while it appeared that the mono-hormonic theory could. It is worthwhile to reiterate Wiesner's (negative) arguments for the mono-hormonic theory:

> But the main objections which were brought against the dihormonic theory, and which caused one to reject it, were derived from its failure to explain adequately and with reasonable economy of hypothesis, certain experimental facts [the wrong medium], observations relating to normal embryonic development [wrong timing] and, last but not least, teratological [intersexual] cases.[87]

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[86] Ibid.

[87] Wiesner, B. P. (1935). "The Post-Natal Development of the Genital Organs in the Albino Rat." The Journal of Obstetrics and Gynaecology of the British Empire **62**: 8 - 75.

The virtue of aesthetic elegance is more difficult to illuminate (as well as illustrate), in part because whats counts as an elegant hypothesis, much like what counts as a descent mousseline, depends upon context, the available "ingredients," and personal and professional taste. Complicating matters further, personal and professional taste are often strongly influenced by the prevailing cultural milliue. Nonetheless, both the mono and the di-hormonic theories can be described as possessing aesthetic elegance of a sort. The di-hormonic theory, in assuming there to be two inductive "stuffs," accords with the presumption of two different physiological developmental endpoints. On the face of it, it makes sense that two different physiologies are the result of two different inducing factors. The mono-hormonic theory, with its presumption of only one active element, proposes a more simple causal pathway.

Likewise, both elaborated hypotheses can claim the virtue of explanatory fertility. In a negative sense, the mono-hormonic theory is "fertile" in that it can answer the problems of media and timing. In a positive sense, the di-hormonic theory accounts for the empirical results of Greene and the "noise" encountered by Wiesner.

In the context of biology (as opposed to that of physics) the virtue of symmetry is difficult to elucidate. Nonetheless, one of the outstanding questions of mammalian sexual development was that of the "asymmetry in potential," a question that inspired Jost's experimental work.

Although, as Simon points out, Hanson does not provide an explicit formal theory of the retroductive process,[88] I claim that a 'formal' (in the sense of universal) logic is not necessary. This is for two reasons. First, as later philosophers point out, different

[88] Simon, H. (1973). "Does Scientific Discovery Have a Logic?" Philosophy of Science **40**(4): 471 - 480.

scientific fields have different methods of confirmation. As such, there can be no singular, explicit 'formal' logic of justification. If there is no formal logic of justification, how can there be an explicit formal logic of discovery? Second, scientific discoveries are made with respect to overarching cognitive goals – goals that vary from field to field, research project to research project. In what follows, I discuss a specific research project: that of Alfred Jost.

IV. Jost's Experimental Confirmation

The mono-hormonic theory was largely experimentally confirmed by Alfred Jost, who, beginning in the late 1940's, worked out the basic mechanisms of sexual differentiation in mammals.[89] Jost was especially puzzled by the fact that the male duct system degenerated without a fetal testis, but the female system could develop in the absence of an ovary, and even develop in male embryos. He wondered why the two systems displayed such different development potentials.[90] Because males have no

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[89] For instance, Jean Wilson writes: "The fundamental mechanism of sexual differentiation of the male and female phenotypes was elucidated by Alfred Jost between 1947 and 1952." In Wilson, J. D. (1989). "Sexual Differentiation of the Gonads of the Reproductive Tract." Biology of the Neonate **55**(6): 322 - 330. Melissa Hines credits Jost with first describing genital feminization in the absence of gonadal hormones in Hines, M. (2004). Brain Gender. New York, Oxford University Press. Finally, Breedlove and Hampson write: "The chain of events during sexual differentiation is well understood in placental mammals such as ourselves, and was largely worked out by Alfred Jost." Breedlove, S. M., and Hampson, Elizabeth (2002). Sexual Differentiation of the Brain and Behavior. Behavioral Endocrinology. B. Becker, Crews and McCarthy. Cambridge, MIT Press.

[90] Jost writes:

> On peut naturellement se demander si cette différence entre les deux sortes de gonoductes ne relève pas de causes plus generales. La persistance des canaux des Müller des femelles castrées est-elle due à une action précoce des ovaires s'exerçant avant le moment de la castration? Pour répondre à cette question, il faudra ovariectomiser des

ovaries, fetal gonadal secretions could not be responsible for the development of the female reproductive system. He speculated that maternal estrogen or perhaps estrogen produced in the male adrenal system might cause female duct development.[91]

Jost's innovative procedural method set the stage for future methodology in the field. He developed his procedure (what Simon calls a class of discovery processes) to achieve the goal of resolving the question of inequality of potential in particular, and, more generally and importantly, the mono- vs. di-hormonic debate.

To resolve the mono versus di-hormonic debate, Jost removed the gonads of rabbit fetuses still *in utero*, before the gonads became sexually differentiated.[92] This technique controlled for the potential influence of fetal gonads on sexual development, and was a marked improvement upon earlier techniques of simply injecting large doses of purified hormones. His approach produced information about the roles played by the embryo's own gonadal hormones.

The results were dramatic. In all the male embryos (which Jost castrated between eighteen and twenty three days of development), the developing Wolffian ducts regressed

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> embryons plus jeunes. On doit cependant remarquer que les canaux des Müller persistent dans les males castres, ce qui donne bien à penser qu'une stimulation ovarienne n'est pas indispensable pour assurer l'évolution des voies femelles.

Jost, A. (1947). "Reserches sur la Differenciation Sexuelle de l'Embryon de Lapin: Role des Gonades Foetales dans la Differenciation Sexuelle Somatique." Archives d'Anatomie Microscopique et de Morphologie Experimentale **36**(4): 18 - 314.

[91] "Mais d'autres secretions expliquent peut-être la persistance des voies Müllériennes: on songe à la folliculine maternelle ou a l'activite des surrenales foetales." Ibid.

[92] "Pour analyser le role endocrine des gonades foetales, on a essaye´ de castrer les embryons ou jeunes individus avant ou pendant la différenciation sexualle somatique." Jost, A. (1946). "Recherches sur la Differenciation Sexuelle de l'Embryon de Lapin: Introduction et Embryologie Genitale Normale." Archives d'Anatomie Microscopique et de Morphologie Experimentale **36**(2): 151 - 194.

as they do in female development. In those castrated the earliest, the structures forming the oviducts, uterus, and part of the cervix developed as if the embryo were female.[93]

In contrast, the female embryos (whose ovaries had been removed) displayed only slightly altered sexual development. Those castrated latest (at twenty-three days) developed as normal females.[94] In those castrated earlier, the oviducts, uterus, cervix and vagina differentiated almost normally, but would not grow to full size if the ovary were removed early enough.[95]

To test the speculation that maternal or adrenal estrogen could cause female development in males, Jost castrated five male embryos, and placed a crystal of androgen (methyltestosterone or testosterone propionate) in place of the fetal testes. He wanted to see if androgen itself would counteract the trend towards female development. Unlike the previous male castrates, these embryos displayed normal masculine development of both the prostate and external genitals.[96] However, the Müllerian ducts did not regress, implying that normal male development relied upon more complicated factors than the mere presence of testosterone.

Jost concluded that the female duct system developed (for the most part) without stimulation by hormones from the embryonic ovary. This would explain how female

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[93] Jost, A. (1947). "Reserches sur la Differenciation Sexuelle de l'Embryon de Lapin: Role des Gonades Foetales dans la Differenciation Sexuelle Somatique." Archives d'Anatomie Microscopique et de Morphologie Experimentale **36**(4): 18 - 314.

[94] "Apres la castration, la femelle se differencie comme une femelle normale (il en a ete de même pour un enbryon castré a 23 j. 20h.)" Ibid.

[95] "La femmelle ovarietomisée acquiert les characteres de son sexe, mais ses organes müllériens sont moins volumineux que normalement." Ibid.

[96] Ibid.

structures could differentiate in both males and females whose gonads had been removed *in utero*. He theorized that, in addition to testosterone, the testes made some substance that inhibited female duct development. (This substance, later called Müllerian Inhibiting Substance or the Anti-Müllerian Hormone, was not chemically isolated until 1986.)

Jost interpreted these results to support the mono-hormonic theory more strongly than the di-hormonic. He noted that the male and female duct systems, while originating from the same basic structure, had different development potentials. Specifically, female development occurs unless actively suppressed, while it appeared that male development occurs only when actively promoted. Regardless of the genetic sex of the embryo, female ducts would develop unless suppressed by a testicular secretion, and male ducts degenerated unless exposed to testosterone.

But Jost's results did not provide unequivocal support for the mono-hormonic theory. Remember that when the ovaries were removed early in fetal development, the female duct system did not grow to normal size. From this, Jost concluded that it was "probable that the ovary also produces a morphogenetic secretion, but there is no doubt that it plays a more limited role than the testicular secretion."[97] In addition, he pointed out that, while ovarian secretions did not cause the breakdown of the male duct system, this was no indication that the ovaries played *no* role in sexual differentiation: they could act as a "double assurance."[98]

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[97] "Il est donc probable que l'ovaire produit également une sécrétion morphogéne, mais celle-ci joue sans doubte un role plus limité que la sécrétion testiculaire." Ibid.

[98] "D'autre part, constater que les ovaires ne sont pas indispensables a la régression des canaux de Wolff par exemple, ne prouve pas que normalement ils ne jouent aucun role: ils pourrait y avoir une 'double assurance'." Ibid.

In other words, Jost's work – that is, Jost's interpretation of his work – did not provide a "crucial experiment" that confirmed wholesale a particular scientific theory, but rather acted as a process of discovery intended to explore the viability of various elaborated hypotheses. But because Lillie's resolution of the freemartin problem was considered crucial, the scientific community's interpretation of Jost's work took on a different flavor.

V. Response of the Scientific Community

In spite of his subtle interpretation of the results, most of Jost's contemporaries understood his experiments to support the mono-hormonic theory. The consensus of the scientific community moved rapidly from an initial, cautious interpretation of the results of Jost's work to an outright acceptance of his work as confirming the mono-hormonic theory. Mandel Schechtman, summarizing investigations of hormone manipulation in the 1949 *Annual Review of Physiology*, notes that the "results of hormone injections indicate relative sensitivities but do not inform us as to factors actually operative in the embryo," although the results of Jost's experiments with prenatal gonadectomy produced "information more pertinent to the latter."[99]

L. G. Wells, reporting on the work of Jost and others in the 1952 *Review*, claims that:

[99] Specifically, the information that the "testis seems to act by secretion since the Wolffian ducts are maintained after unilateral, thought not after bilateral, castration." Schechtman, A. M. (1949). "Developmental Physiology." Annual Review of Physiology **11**: 1 - 17.

> [I]t has been virtually proven that the testes of fetal rats produce a hormone (androgen) which stimulated the prenatal growth of the genitalia . . . it is reported [by Jost] that in some cases the genitalia of castrated fetuses are feminized.[100]

However, in spite of his acceptance that prenatal testes produce androgen:

> The reviewer believes that it remains to be determined whether the first production of testicular androgen antedates (a) the earliest step in the differentiation of the accessory reproductive organs and (b) the "modulation" of the primordia of these organs.[101]

This skepticism soon disappeared. By 1954, "androgen production by the fetal testes has gained support,"[102] and in 1959 the "pituitary gonadotrophins [released while in utero] are indispensable for testicular functions."[103] By the 1960's, most scientists accepted that androgens were (solely) responsible for the transformation of an undifferentiated fetus into a male. For instance, the 1961 edition of *Sex and Internal Secretions* relies heavily on Jost's results to explain sexual differentiation in mammalian embryos, concluding that:

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[100] Wells, J. L. (1952). "Growth." Ibid. **14**: 31 - 43.

[101] Ibid.

[102] Leathem, J. H. (1954). "Reproduction." Ibid. **16**: 445 - 459.

[103] Caldeyro-Barcia, R., et. al. (1959). Ibid. **21**.

> Altogether, the evidence clearly indicates that the male hormone is the essential determining factor in the survival and sexual differentiation of the male sex ducts and seminal vesicles. Notwithstanding the minor exceptions noted above [having to do with a particular species of marsupial], the female hormone evidently has little role.[104]

Jost himself later referred to females as the "neutral" sex type. At a conference more than two decades after he initially published his findings, he claims the "genital structures obey an inherent trend (or programme) for femaleness, unless the fetal testes oppose the feminine programme and impose a masculine orientation."[105] Females become females because they *lack* testes.

The reaction of the scientific community brings up two questions. First, why was the acceptance so rapid? Scientists are usually more hesitant to adopt one particular theory over another based on a single series of experiments performed by one individual. Second, why did so many endocrinologists and biologists interpret Jost's work as unequivocally supporting the mono-hormonic theory?

The answers to these questions lie in the fact that many researchers at this time considered the two hormonic theories to be completely incompatible and the fact that the

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[104] Burns, R. K. (1961). Role of Hormones in the Differentiation of Sex. Sex and Internal Secretions. W. C. Young. Baltimore, The Williams and Wilkins Company. **I:** 76 - 158. In addition, the author of a 1960 endocrinology text book, citing Jost, writes:

> The experiments on fetal castration indicate strongly that in placental mammals the testis plays the principle part in differentiating the sexes. In the absence of the testis, as in normal females and castrated fetuses of either sex, the female type is realized.

Turner, C. D. (1960). General Endocrinology. Philadelphia, W. B. Saunder Company.

[105] Jost, A. (1979). Sexual Trends in Vertebrate Development. Ciba Foundation Symposium, London, Excerpta Medica.

crucial resolution took place before, not after, Jost's work.[106] As such, Jost was perceived by many[107] as providing empirical support for the crucial resolution (mono-hormonic theory), and that support provided no reasons for a "compromise theory."

For instance, Wells, in the 1952 *Annual Review of Physiology*, describes Jost's conclusion as:

> A recent view of sexual differentiation in mammals is (a) that the testicular secretion induces the formation of the "male genitalia" and prevents the appearance of "female genitalia"[108] in males; (b) that the action of the testicular secretion is largely local or unilateral; and (c) that the embryonic ovaries do not influence sexual differentiation.[109]

Wells describes this view as "problematic" because of experiments wherein gonadectomized female laboratory animals, when injected with androgens, "fails to

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[106] In addition to other reasons. Helen Longino, in *Science as Social Knowledge* (1990), argues that mono-hormonism was accepted, in part, because it reaffirmed cultural the tropes of masculine activity and feminine passivity.

[107] Not all, of course. In their introduction to the 1953 Annual Review of Physiology, Krohn and Zuckerman write:

> In spite of extensive studies on intersexuality, the new chapter [of the Review] also shows that the freemartin condition in cattle has still not been reproduced experimentally in the lab, and that the role of maternal and foetal sex hormones in the embryonic differentiation of the reproductive tract remains a controversial topic.

Krohn, P., and S. Zuckerman (1953). "Reproduction." Annual Review of Physiology **15**: 429 - 455.

[108] By which Wells means the Mullerian ducts.

[109] Wells, J. L. (1952). "Growth." Annual Review of Physiology **14**: 31 - 43.

prevent the formation of derivatives of the Müllerian ducts."[110] In addition, other experiments demonstrated that androgen injections were effective in inducing masculinization no matter where they were injected (that is, androgenic influences were not limited to specific areas).

On the other hand:

> [T]he conception that the ovaries fail to influence differentiation is acceptable despite the report that the destruction of the ovaries of fetal mice by irradiation is followed, in some cases, by a failure of retrogression of the lower portion of the Wolffian ducts.[111]

In other words, Jost's "default" model is acceptable in spite of its inability to explain certain anomalies. On this approach, anomalies (such as androgen failing to prevent the development of Müllerian ducts) become experimental "noise."

More generally, Jost's work was seen as providing confirmation of the commonly accepted interpretation of Lillie's work. This interpretation of Jost's work, especially the model of female development as the result of a lack or absence of hormonal influence, is widely accepted to this day.[112] In an issue of *Biology of the Neonate* devoted to the influence of Jost, Jean Wilson writes:

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[110] As mentioned earlier, Jost suggested that the embryonic testes secrete a substance that inhibits the formation of the Müllerian ducts – a suggestion which turned out to be correct.

[111] Wells, J. L. (1952). "Growth." Annual Review of Physiology **14**: 31 - 43.

[112] Capel and Coveney write:

> Meanwhile, basing a set of experiments on the theories set forth by Lillie, Alfred Jost developed the Jost paradigm, which has directed the field ever since. Jost showed that while a testis placed near the genital ducts of a female would support development of the Wolffian duct and induce regression of the Müllerian duct, a crystal of testosterone,

> According to the Jost formula – now the central dogma of sexual development – sexual differentiation is a sequential, ordered, and relatively straightforward process. Chromosomal (or genetic) sex, established at the time of conception, directs the development of either ovaries or testes. If testes develop, their hormonal secretions elicit the development of the male secondary sex characteristics, collectively known as the male phenotypes. If an ovary develops or if no gonad is present, anatomical development is female in character.[113]

This demonstrates not only the strong influence of Jost, but the interpretation of his work as an unequivocal confirmation of the mono-hormonic theory. This interpretation of Jost's default model is more sophisticated than its original form: it is not simply the presence of the testes, but of the genetic precursor to the testes that is responsible for sexual differentiation. This more sophisticated form of the default model is still espoused in a number of contemporary endocrinology textbooks.[114]

> though capable of inducing many aspects of male differentiation, did not lead to the degeneration of the Müllerian duct. These experiments strongly argued for the existence of a discrete substance produced by the testis that caused Müllerian regression and was capable of exerting a freemartin-like effect on the ovary.

Capel, B., and Coveney, Doug (2004). "Frank Lillie's Freemartin: Illuminating the Pathway to 21st Century Reproductive Endocrinology." Journal of Experimental Zoology **301A**: 853 - 856.

[113] Wilson, J. D. (1989). "Sexual Differentiation of the Gonads of the Reproductive Tract." Biology of the Neonate **55**(6): 322 - 330.

[114] In *Behavioral Endocrinology*, S. Marc Breedlove and Elizabeth Hampson write:

> Early in development, both XX and XY individuals have gonads that do not yet resemble either testes or ovaries, and are therefore called "indifference gonads." The one crucial task performed by at least one gene on the Y chromosome [called the sex-determining region of the Y (Sry)] is the transformation of this originally indifferent gonad into a testis . . If the cells of the indifferent gonad contain a Y chromosome with the Sry gene, they begin to develop as a testis. In the absence of a Sry gene, the gonad will develop as a ovary.

In addition, many scientists outside the field of endocrinology adopted the Jostian default model. This includes not just biologists in general,[115] but psychologists as well. As will be discussed later, an important extension of Jost's default model of genital development is that of applying it to brain development.[116] Developmental psychologist June Reinish, reflecting upon recent research and models concerning the effect on behavior of prenatal gonadal hormones, proposes the following hypothesis:

> During the fetal period, the androgens have a fundamental influence on the organization and differentiation of the neural tissues (substratum) designed to mediate, at least partially, dimorphic behavior in human males and females.[117]

Note that it is the androgens that do the organizing – not just of the genital tissues but of the brain itself. This updated version of the mono-hormonic hypothesis has the advantage of simplicity. Instead of two causal agents in the general theory of eitiology,

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Breedlove, S. M., and Hampson, Elizabeth (2002). Sexual Differentiation of the Brain and Behavior. Behavioral Endocrinology. B. Becker, Crews and McCarthy. Cambridge, MIT Press.

[115] E. g., Carlson, B. (1999). Human Embryology and Developmental Biology. St. Louis, Mosby.

[116] One textbook author writes:

> In most mammal studies to date, the brain in either sex is feminine until it is converted to a masculine form in males through the action of testosterone. This masculinization, or defeminization, of the brain affects not only sexual behavior but also a wide range of behaviors relating to aggression, play, and ingestions, as well as a number of key physiological processes.

in Schulkin, J. (1999). The Neuroendocrine Regulation of Behavior. New York, Cambridge University Press.

[117] Reinish, J. M. (1974). "Fetal Hormones, the Brain, and Human Sex Differences: A Heuristic, Integrative Review of Recent Literature." Archives of Sexual Behavior **3**(1): 51 - 91.

there is only one. This extension of the Jostian model of genital development to brain development forms the theoretical foundation for the development of behavioral endocrinology as a particular subfield of endocrinology.

As may be apparent from this extension of the Jostian model, many scientists accept it as the theoretical foundation for further research. Wilson writes:

> This paradigm has had a profound impact on biology and medicine and has influenced all subsequent investigations in this field . . . this discussion has been designed to focus on some specific aspects of this impact . . . and the current challenge to explain the Jost model in molecular terms.[118]

By "paradigm," Wilson does not mean a world-view in the Kuhnian sense, but rather as the foundation of a disciplinary matrix. The desire to explain Jost's model in terms of genetic and molecular mechanisms is a reasonable consequence of the "genetic revolution" that occurred shortly after Jost published his findings.

Thus far, I've demonstrated that the process of discovery – from the initially postulated elaborated hypotheses of mono- and di-hormonism, to the experimental procedures for Jost – that eventually led to the adoption of mono-hormonism was not capricious, but based on good reasons. One might even claim that, given the specific goals of endocrinologists at this time, it was logical.

VI. Scientific Goals and the Logic of Method

[118] Wilson, J. D. (1989). "Sexual Differentiation of the Gonads of the Reproductive Tract." Biology of the Neonate **55**(6): 322 - 330.

What does it mean for a method – either of discovery or of justification – to be logical? Most generally, we consider a method or process to be "logical" if it satisfies certain procedural norms established for it. These norms, in turn, derive from our concern that the method accomplish the purpose for which it was established in an efficacious manner.

Simon defines the logic of scientific method, in general, as consisting of a normative set of standards for judging the processes used to discover or test scientific theories. One implication of this definition is that the norms can be derived from the goals of scientific activity. If this is the case, we can generalize the logic of scientific method as follows:

Let

G = a particular goal of discovering valid scientific laws
P = a class of discovery processes (with p ϶ P)
C = set of conditions (with c ϶ C)

The set of conditions can be attributed to processes, such that c(p) is a function from C X P to dichotomous truth-values. If, for all c, c(G ⊃ c), C is a set of norms for P with respect to G. In other words, if the attainment of goal G implies that the conditions, C, be satisfied, then we ought to employ the process p that satisfies C.[119]

Simon claims that:

[119] Simon, H. (1973). "Does Scientific Discovery Have a Logic?" Philosophy of Science **40**(4): 471 - 480.

> If G is the goal of discovering valid scientific laws, and P is a class of discovery processes, then C provides a normative theory of scientific discovery. If G is the goal of testing the validity of proposed laws, and P is a class of test procedures, then C provides a normative theory of testing laws.[120]

As such, the logic of scientific method is, in general, the same for both the process of discovery and justification. For those scientists attempting to discover the mechanisms of hormone action, the discovery processes consisted of proposing hypotheses that could explain the physical phenomena while, at the same time, embody the explanatory virtues mentioned by Hanson. For instance, Ross Harrison, in his discussion of the general problem of embryonic "determination" (development), points out that the field of experimental embryology "will be placed on a sounder basis" if the questions addressed by researchers are more broadly framed:

> In dealing with such a complex system as the developing embryo it is futile to inquire whether a certain organ rudiment is "determined" and whether some particular feature of its surroundings, to the exclusion of others, "determines" it. A score of different factors may be involved and their efforts most intricately interwoven. In order to resolve this tangle we have to inquire into the manner in which the system under consideration reacts with other parts of the embryo at successive stages of development and under as great a variety of experimental conditions as possible to impose. Success will be measured by the simplicity,

[120] Ibid.

> precision and completeness of our descriptions rather than by a specious facility in ascribing causes to particular events.[121]

Harrison calls for explanations that are not only empirically adequate, but also simple and broad in scope. In other words, the process of discovery of developmental hypotheses should conform to Wiesner's ideal of "economy of hypothesis." We have seen this general ideal – or normative theory – at work in both the formulation of the mono- and di-hormonic theories, as well as in Jost's experimental confirmation.

Simon points out that norms can have either a logical or an empirical basis. For instance, when playing the game of tic-tac-toe, a move that puts a second cross at the intersection of two unblocked arrays, each of which has one cross already, is an optimum (winning) move. As such, a normative procedural theory of tic-tac-toe recommends strategies that make facilitate such a move, when possible. The adequacy of this condition can be deduced solely from the rules of tic-tac-toe.[122]

In contrast, a norm of chess strategy – that one should consider attacking the King only when superior mobility has been achieved – is an empirical rule. That it, it has been established as a norm based upon the cumulated wisdom of centuries of chess players, rather than a deduction from the rules of chess alone.[123] Because it does not come with a stringent pre-established set of rules, the field of biology is more akin to the game of

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[121] Harrison, R. (1933). "Some Difficulties of the Determination Problem." American Naturalist **67**(711): 306 - 321.

[122] Simon, H. (1973). "Does Scientific Discovery Have a Logic?" Philosophy of Science **40**(4): 471 - 480.

[123] Ibid.

chess than that of tic-tac-toe. As we shall see, crucial resolutions build upon each other, forming a sort of "cumulated wisdom," although not one of centuries.

Simon speculates that, because of the presence of an empirical component in norms, those philosophers who subscribe to the sharp descriptive/normative distinction might entertain the notion that certain processes cannot be the subject of logical analysis, but only that of description. He has two responses to this. First, if the notion of logical analysis is interpreted broadly, one can undertake a normative logical analysis of any goal-directed process. Second, upon a narrow interpretation – that of excluding deductions from empirically based premises – the dichotomy between logical analysis and description is false.[124]

Simon points out that the use of a recommended strategy in pursuit of a goal does not guarantee the achievement of that goal.[125] While the goal appeared to be achieved with the resolution of the mono- vs. di-hormonic debate, such is not the case with other elaborated hypotheses in the history of endocrinology (as we shall see in later chapters.) In spite of potential failures, Simon claims that there can be – in fact, there is – a logic of discovery.

Why have philosophers of science, in general, shied away from the possibility of a logic of discovery? Simon suggests that this reticence is due to the assumption that any logic of discovery invokes the long-standing philosophical problem of induction. As a

[124] Ibid.

[125] Ibid.

result, philosophers would prefer to cut through the Humean knot, rather than untangle it.[126]

Simon also claims that this problem, vis a vis the process of *discovery*, is misappropriated:

> Law discovery means only finding pattern in the data that have been observed; whether the pattern will continue to hold for new data that are observed subsequently will be decided in the course of testing the law, not discovering it.[127]

In other words, Humean concerns about induction apply to the process of *justification*, not the process of discovery. Given the limited nature of data sets, justification is an ongoing – and perpetually incomplete – process.

Simon proposes to banish the problem of induction from the process of discovery by defining:

A *law-discovery process* is a process for recoding, in a parsimonious fashion, sets of empirical data.

A *normative theory of scientific discovery* is a set of criteria for evaluating law-discovery processes.[128]

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[126] The phrase Simon uses is "untie the Gordian knot of induction." Ibid.

[127] Ibid.

[128] Ibid.

It is apparent that, for Simon, the parsimonious recoding of data sets is not equivalent to simple induction upon those sets. But if we can give a descriptive account of how scientists make such discoveries, *and* a normative account of the means by which they make them, then, according to Simon, we have constructed a logic of discovery. Unfortunately, Simon does not elaborate on what he means by the terms 'recoding' and 'parsimonious.'[129]

However, several examples from the history of endocrinology can help to clarify these terms, the debate between mono- and di-hormonic theories of development being one of them. Both the mono- and the di-hormonic theories recode data sets in a parsimonious fashion, albeit in different ways. The "parsimony" of the di-hormonic theory has the advantage of explanatory completeness: it recodes the data sets in such a fashion so as to explain laboratory findings while respecting the initial (dichotomous) gendered assumptions about the nature of hormones. The "parsimony" of the mono-hormonic theory is more abstract: its invocation of a more simple causal pathway reflects the virtue of explanatory "simplicity" triumphed by researchers such as Harrison.

But what of Simon's normative theory of scientific discovery? In the history of endocrinology, this involves not the testing of laws, but the crucial resolution between elaborated hypotheses. Although Simon does not elaborate on the criteria for evaluating law-discovery processes, presumably this involves the comparison of different methods of parsimonious encoding. But this, again, brings to the fore Humean problems of induction.

[129] This isn't exactly true: he uses examples amenable to computational recoding. Unfortunately, the practice of biology is, in this respect, significantly different from the practice of knitting.

Simon points out that, traditionally, the logic of justification was thought to rest on deductive logic, while any normative theory of discovery has been thought to require a quite different logic as its foundation: that of induction.[130] Were this to be true, the logic of discovery would inherit the philosophical difficulties of induction.

As an initial response to this problem, Simon provides a concrete example of discovery which, he claims, does *not* rely on induction. Consider the following sequence:

ABMCDMEFMGHMIJMKLM

MNMOPMQRMSTMUVMWXMYZMABMC . . . .

If we know our alphabet, we can see a pattern. In particular, "it is redundant, and can consequently be described more parsimoniously by defining the pattern than by exhibiting the sequence itself."[131] In particular, the pattern can be described in terms of triples: the first two letters in each triple progress through the alphabet, with the third being "M." We can schematize this pattern as follows:

(1) $n(\alpha)n(\alpha)s(\beta)$; $\alpha = Z, \beta = M$

[130] Simon, H. (1973). "Does Scientific Discovery Have a Logic?" Philosophy of Science **40**(4): 471 - 480.

[131] Ibid.

Where ‘n(α)’ means replacing a letter by the letter next to it on the alphabet, α; ‘s(β)’ means repeating the same letter as β; while the expressions ‘α = Z’ and ‘β = M’ set the initial values on the alphabets, at Z and M, respectively.[132] As such, Simon claims that the normative theory of discovery processes can be viewed as a branch of computational theory.

One (anonymous) reviewer of an early draft of this paper objects that Simon uses examples that prejudice the argument in his favor. Specifically, the range of alternatives is already delimited. Simon replies that this objection rests on the distinction between “well-structured” problems and “ill-structured” problems. This distinction, he claims, recalls the Kuhnian distinction between normal and revolutionary science.[133]

There are several problems with Simon’s reply to this objection, especially vis a vis the field of endocrinology. First, it is not clear that the distinction between well-and-ill structured problems is a valid one. Second, it is not clear how this maps onto Kuhn’s distinction between normal and revolutionary science.

Say, for the sake of argument, that well-structured problems are those amenable to computational analysis and, as such, can be distinguished clearly from ill-structured problems. On this account, problems within the field of endocrinology are ill-structured. In particular, etiological theories of development cannot be recoded as schema like the type of (1). Earlier researchers did not know the “alphabet” of hormones: elucidating not just the number but also the nature of these internal secretions was the order of the day. Even after hormones came to be defined in terms of chemical composition, it was not

[132] Ibid.

[133] Ibid.

clear how these hormones had an "order." (As we have seen, one of Jost's goals was to determine the chronological "order" – that is to say, timing – of the various hormones in order to solve the riddle of inequality of potential.)

Even if the problems in endocrinology could be described as well-structured, the Kuhnian distinction between normal and revolutionary science does not hold for endocrinology. Competing elaborated hypotheses do not present alternative world-views, but build upon earlier research, theorizing, and general presuppositions. As such, the choice between them does not rely upon a potentially irrational gestalt-switch, but invokes ideals of explanatory virtue.

VII. Conclusion

Just as there is a logic of discovery to the formulation of elaborated hypotheses, there is also a logic to the crucial resolutions between them. Elaborated hypotheses are not merely irrational, creative, or mystical suggestions, but attempts to explain a particular problem in a reasonable, albeit ultimately limited, fashion. Likewise, crucial resolutions also possess a logic of discovery (rather than a purely empirical logic of confirmation) in that they are proposed in advance of unambiguous empirical evidence.

As seen in the case of Jost, the process of discovery can strongly influence the process of confirmation. The general explanatory goals of endocrinological research – answering the largest number of conceptual problems with the greatest economy of hypothesis – inform not just the formulation of elaborated hypotheses but also the

interpretation of empirical results. As such, Lillie's resolution of the freemartin problem was seen as crucial after the fact, and Jost's work was seen as unambiguous confirmation of the mono-hormonic theory, in spite of both authors' subtle and cautious interpretations of their own results.

That the mono- vs. di-hormonic debate was resolved through a crucial resolution implies that the "logic" of discovery involves more than simple empirical confirmation or disconfirmation. The choice between elaborated hypotheses, while not capricious, cannot be explained by appeal to crucial *experiments*. Rather, the process (and logic) of discovery "blurs in" to the process (and logic) of confirmation.

To reinforce this point, the following chapters examine another crucial resolution in the history of endocrinology: that of the etiology of sexual behavior.

Chapter 4

Of Rats and Men: From the Bisexual to the Heterosexual Model of Sexual Behavior

I. Introduction

From the 1920s to the 1940s, there were two main areas of controversy in endocrinology: whether estrogen plays any developmental role in the formation of the fetus; and whether all mammals have the potential to display both masculine and

feminine behavior. That is, whether mammals, when born, have the capacity to display behaviors typical of either sex, or if there is an "inequality of potential" wherein animals are predisposed towards behavior specific to their anatomical sex. This second controversy concerns the development of sexual and gendered behavior: whether these behaviors require socialization to be manifested, or are "hardwired" in during fetal development.

This controversy, like the one discussed in the previous chapter, was resolved through a crucial resolution. The first crucial resolution, that of the freemartin problem, inspired Jost's research program. This research program (and, in particular, its mono-hormonic interpretation) defined the basic physiological mechanisms that served as a foundation for the crucial resolution of the second controversy. Animal models developed in attempts to resolve this second controversy are the primary source for the current general explanatory model of human sexual and gendered behavior.

Sexual development involves more than anatomy. It also involves development of behavioral characteristics that allow an individual to compete for mates, and produce, rear, and protect young. After the basics of anatomical sexual development had been largely worked out (by Jost), the next target for endocrinological investigation was the development of sexual behavior. At this time, there were two general hypotheses concerning the origination of sexual behavior: (1) that sexual behavior requires socialization to be manifested and thus implying that all mammals are undifferentiated at birth in terms of predispositions towards sexual behavior; and (2) that sexual behavior is innate (in the sense that most mammals are predisposed to display the behavior typical of their sex).

In time, the majority of endocrinologists rejected the first hypothesis in favor of the second, which remains to this day the dominant explanatory model of mammalian sexual behavior. To understand why this happened, a bit of intellectual history is in order. In what follows, I outline the historical progression of the development of two competing hypotheses of animal sexual behavior, as well as the implications each has had for conceptions of human sexual and gendered behavior, focusing on the work of Frank Beach and William Young. My goal is to provide an outline of the lines of evidence and reasoning endocrinologists used to arrive at the current explanatory model.

The lines of evidence and reasoning bear a structural similarity to those used to resolve the first dispute, with some important differences. The debate concerning the etiology of sexual behavior was a debate between two *general*, rather than elaborated hypotheses, and thus was not as sharply defined as that between mono and di-hormonism. Until 1959, the debate was framed as between the influences of external factors (the environment in general, socialization in particular) versus those of internal factors (genetics and hormones) on behavior.

As such, the controversy concerned a general question about the etiology of behavior, not persistent anomalies and conflicting experimental results, as was the case with the mono versus di-hormonic debate. But there was one specific question that had elaborated (and conflicting) hypotheses as well unclear (and conflicting) experimental results: the etiology of homosexuality. The crucial resolution of this question is the topic of the next chapter.

In what follows, I give some historical background concerning the importance of the emerging field of endocrinology and its contribution to the general debate, present

some initial hypotheses about the etiology of sexual behavior, and lay out the intellectual history leading up to the crucial resolution. This intellectual history is necessary to understand the crucial resolution itself, with the intention of showing how it instigated the rapid acceptance of one general hypothesis over the other. Indeed, like the resolution of the freemartin problem, it was accepted in advance of convincing empirical evidence (or, for that matter, any evidence at all) and influenced subsequent developments in the field of endocrinology.

In addition to reinforcing the conclusions about crucial resolutions made in the previous chapter, I present some general conclusions about the methodologies discussed that have philosophical implications. In the course of its development, the field of endocrinology has concerned itself with uncovering the causal pathways behind certain behavioral outcomes. However, this general research program, as a result of encountering explanatory obstacles, has been forced to shift its attention from behaviors *per se* to capacities supporting behaviors. This shift from behaviors to capacities was an attempt to delineate the respective influences of internal ("natural," "innate") factors and external ("environmental," "socialization") factors upon development.

II. Frank Beach and the Importance of Learning

Human models of endocrinology, particularly models of hormonal influences on sexual and gendered behavior, draw most of their force from rodent studies.[134] Scientists in the field of behavioral endocrinology use results from experimental manipulation of rodent hormones to construct mechanisms that explain sex differences in behavior and cognitive ability in biological terms.

From the mid 1930s to late 1940's, Frank Beach, one of the founders of modern behavioral endocrinology, accomplished three tasks: he determined and quantified behaviors that could be designated as masculine or feminine (including, but not limited to, lordosis and mounting); developed some sense of the behavioral differences among different species and among individuals of the same species; and studied the effects of gonadal steroids on adult sexual behaviors.[135] In synthesizing the results of these investigations, he articulated a model of the origins of animal masculinity and femininity, a model that was promptly applied to humans.

Beach argued that, neurologically, all animals have a bisexual potential. By "bisexual," he meant that female rats had the potential to behave like males during mating, and vice versa. (Later researchers refer to this type of behavior as, rather

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[134] In their 1954 review, Beach and Jaynes claim that their effort:

> [S]eems worth doing not only because of its usefulness to students of animal behavior, but also because scientists interested primarily or exclusively in human psychology very frequently turn to the literature dealing with lower animals in connection with discussions of human development.

Beach, F. A., and Julian Jaynes (1954). "Effects of Early Experience Upon the Behavior of Animals." Psychological Bulletin **51**(3): 239 - 263.

[135] See Young, W. C. (1961). The Hormones and Mating Behavior. Sex and Internal Secretions. W. C. Young. Baltimore, The Williams and Wilkins Company. **II**.; Goy, R. W. a. M. R. (1991). Heterotypical Behaviour in Female Mammals. Heterotypical Behaviour in Man and Animals. H. B. Aron. London, Chapman and Hall.; and Marler, P. (2005). "Ethology and the Origins of Behavioral Endocrinology." Hormones and Behavior **47**: 493 - 502.

confusingly, 'heterotypical behavior,' that is, behavior typical of the opposite sex.) Beach observed a large amount of bisexual behavior in his lab animals, and wanted to know what biological factors lead to particular sexual expressions, whether they be heterosexual matings, male-male mounting, male lordosis, and female-female or female-male mounting.

However, this does not mean that rodents were just as likely to display behavior typical of the opposite sex as that of the same sex. From his studies of castrated male rats, he concluded that "in the genetic male the threshold of responsiveness in the neural circuits for masculine coital performance is inherently lower than the threshold in the mechanisms for feminine behavior."[136] In other words, males displayed a stronger behavioral response to androgens then they did to estrogens.

Beach emphasized the importance of environmental influences on behavior, especially in regards to learning. In a paper about the influence of early experience, Beach notes that:

> Many psychologists appear to conceive of learning ability in animals as genetically determined and relatively unmodifiable, but recent findings indicate the untenability of this thesis.[137]

A spate of studies at this time resulted in the discovery that "far from being purely "instinctive," (like the scratch reflex) the reactions of animals to others of their own kind

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[136] Beach, F. A. (1947). "A Review of Physiological and Psychological Studies of Sexual Behavior in Mammals." Physiological Reviews **27**: 240 - 307.

[137] Beach, F. A., and Julian Jaynes (1954). "Effects of Early Experience Upon the Behavior of Animals." Psychological Bulletin **51**(3): 239 - 263. One such psychologist was W. Kohler.

are in part dependent upon individual experience and learning which typically occurs in infancy."[138] This process is similar to, but more complicated than, the phenomenon of "imprinting" commonly seen in very young birds. After discussing a number of experiments that studied behavior after restricting visual or tactile stimuli, Beach concludes that:

> They point to the fact that even the simplest elements in the total behavioral repertoire are normally a product of early experience and therefore interference with the accumulation of such experience may profoundly alter adult activities. These experiments also make one suspect that more complex forms of behavior will be found to depend very heavily upon habits formed in early life.[139]

A series of investigations support the latter claim. Female rats, when raised in an environment where nothing could be picked up or carried, failed to build nests for their first litters, even though building material was available. Likewise, females raised under conditions that prevented self-grooming failed to clean their young upon delivery. Similar studies of chimpanzees (restricting their access to playthings) reinforced the notion that early experience matters greatly for a wide range of behavior.[140]

As the above-mentioned experiments with rats imply, not only does adult sexual behavior depend upon hormonal stimuli, it also depends on early experience. In making

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[138] Beach, F. A. (1953). "Animal Research and Psychiatric Theory." Psychosomatic Medicine **15**(5): 374 - 388.

[139] Ibid.

[140] Ibid.

this claim, Beach is rejecting the common assumption at the time that sexual behaviors are primarily instinctive:

> Among the most species-specific behavior patterns in any particular species are those having to do with reproduction – courtship, fertilization, nest building, parturition, and the care of the young. For a long time, these often unique stimulus-response organizations were classified as "instincts" and were thought to be exclusively determined by genetic constitution. Evidence which shows that the occurrence of these responses is heavily dependent upon other factors, especially the early experience of the animal, has recently been gathered from many widely divergent invertebrate and vertebrate species.[141]

One might wonder what motivated Beach and his colleagues to raise females in an environment where nothing could be picked up, in order to investigate nest-building behavior. Likewise, one might wonder why they prevented young females from being able to groom themselves, in order to investigate pup-grooming behavior. On the face of it, both lines of investigation appear extreme. According to Beach's general hypothesis, all that the organization of sexual capacities requires is socialization, with the attendant learning. Indeed, Beach's early experiments (merely) investigated the effects of social isolation.

Beach's rejection of the simple claim that sexual behaviors are solely due to instinct provides a hint about his motives in the afore-mentioned restriction experiments. Here it is important to note an ambiguity in the language of these early reports: socialization is assumed to carry learning in its wake, but the (assumed) key factor is the

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[141] Beach, F. A., and Julian Jaynes (1954). "Effects of Early Experience Upon the Behavior of Animals." Psychological Bulletin **51**(3): 239 - 263.

learning. It is not immediately obvious that socialization is the only vector for early learning, as there are many other kinds of early experience. I suspect that Beach's group began to doubt that learning occurred only through socialization, and were inspired to control for factors other than early social contact. If early learning were the key causal factor for developing later capacities, "interference with the accumulation of such experience may profoundly alter adult activities,"[142] as Beach notes.

However, Beach does not claim the etiology of sexual behavior is solely determined by environmental influences. His is a more nuanced claim:

> It is worth stressing at this point that early experience appears to influence the kinds of stimuli that will later evoke reproductive activities, whereas the actual responses are less subject to modification.[143]

In support of this claim, Beach noted that partially decorticated male rats, when placed with estrous females, copulated in fewer tests. But the number of copulations during each positive test was not affected. Beach interpreted this to mean that decortication decreased arousal potential, but did not affect the actual copulatory pattern. Motor patterns of copulation were described (by Beach, among others) as being "innately organized."

To account for the influence of both instinct and learning, Beach divided sexual behavior into two broad components: capacity for sexual performance and susceptibility to sexual arousal. Decoricated rats had a lower arousal susceptibility (thought to be

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[142] Beach, F. A. (1953). "Animal Research and Psychiatric Theory." Psychosomatic Medicine **15**(5): 374 - 388.

[143] Beach, F. A., and Julian Jaynes (1954). "Effects of Early Experience Upon the Behavior of Animals." Psychological Bulletin **51**(3): 239 - 263.

controlled by the forebrain), but decortication did not interfere their capacity for sexual performance (thought to be mediated in the brain stem).

Capacity for performance involves not just instinctive motor patterns, but also, according to Beach, a learning process. This process must take place during a critical period in development in order to successfully organize mating behavior. If mating behaviors are not learned in this critical period, they will never be acquired.

His hypothesis accounted nicely for individual variability within each sex, as well as for the fact that both sexes could, under some conditions, display both masculine and feminine mating patterns, and, finally, that both androgen and estrogen could induce either of these patterns in either sex. One result of Beach's model of sexual development was that he considered bisexual and homosexual behavior to be variations within a spectrum of behavior, rather than aberrations or abnormalities.[144] In other words, the "atypicality" of bisexual and homosexual behavior is that of frequency, not pathology.

In spite of Beach's emphasis upon the continuum of sexual development and behavior, many endocrinologists and scientists in general continued to subscribe to the "exemplar" notion of sexual developmental endpoints, wherein any deviation from said exemplar results from a mismatch of gendered elements. Even those researchers sympathetic to the civil and social rights of homosexuals (with rare exceptions) used the terminology of pathology – a terminology rooted in the notion that any sort of mixing of masculine and feminine elements is inherently "unnatural" or pathological. For example, in his 1945 discussion of "hermaphrodites," Albert Ellis notes that:

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[144] In later years, Beach cautioned his fellow scientists against naively applying animal models to human behavior, as well as the assumption that "homosexual" behavior in any species is inherently abnormal. See, for instance, Beach, F. A. (1978). Animal Models for Human Sexuality. Symposium on Sex, Hormones and Behaviour, London, Excerpta Medica.

> It is particularly on this question [of homosexuality] of why some individuals become overtly homosexual – and why others do not – that the study of the sexual psychology of human hermaphrodites may shed much light. For the study of hermaphrodites fortunately provides us with the materials of three crucial human experiments: first, the raising of somatic males and somatic females to act and think as members of the opposite sex to which their bodies and sexual apparatus tend; second, the raising of somatically mixed, masculine and feminine individuals as males, in some cases, and females in others; third, the raising of physiological males or females as members of one sex and later as members of the other.[145]

In Beach's scheme, males and females differed quantitatively but not qualitatively. In other words, he did not take an essentialist approach to masculinity or femininity, nor did he view males and females as pseudo-natural kinds. He observed that "the masculine mating pattern is called forth in females by the same stimuli which evokes it in males, while the feminine responses of males are elicited by those external events which normally initiate these reactions in the female."[146] He noted that androgens increased the sensitivity to external stimulations that brought about masculine mating responses; likewise, estrogens increased the sensitivity of mechanisms for feminine responses. However, this does not mean that rodents were just as likely to display behavior typical of the opposite sex as that of the same sex. From his studies of castrated male rats, he concluded that "in the genetic male the threshold of responsiveness in the

[145] Ellis, A. (1945). "The Sexual Psychology of Human Hermaphrodites." Psychosomatic Medicine **7**(2): 108 - 123.

[146] Beach, F. A. (1947). "A Review of Physiological and Psychological Studies of Sexual Behavior in Mammals." Physiological Reviews **27**: 240 - 307.

neural circuits for masculine coital performance is inherently lower than the threshold in the mechanisms for feminine behavior."[147] In other words, males displayed a stronger behavioral response to androgens then they did to estrogens.

As will be discussed later, Beach's model of animal sexual behavior was quickly abandoned by the scientific community, without being definitively refuted, and replaced with more restrictive readings of animal sexuality. By the late 1950's scientists began importing Jost's "default" model of physical sexual development into the study of behavior. Beach's model of animal sexual behavior was supersceded by what became known as the "organization/activation" model. But first, I examine the historical development of this competing model.

III. William Young and the Influence of Genes

Beach's model dominated the field of behavioral endocrinology at this time. One research group that accepted it was that of William Young and his graduate students (including Elliot Valenstein, Charles Phoenix and Robert Goy). Where Beach investigated the causes of variations in behavior, Young wanted to discover the causes behind the relative *homogeneity* of animal behaviors. While Young accepted Beach's general model, he was more interested in exploring genetic components of behavior. This, he thought, could explain the overall stability in behavior patterns.

[147] Ibid.

If the overall stability of sexual behaviors had a genetic (rather than hormonal) basis, variations in sexual behavior also could be due to genetic factors. To investigate this, Valenstein et. al. compared the behavior of inbred guinea pigs to that of heterogeneous controls. They were concerned that genetic variations might obscure the effects of hormonal variation.

They found that the inbred guinea pigs performed in a more homogeneous fashion than did the controls, suggesting a genetic basis for behavior. Valenstein et. al. are cautious to not claim that sexual behavior is just a matter of genetic influence: "Although alternative explanations cannot be excluded, the possibility that the character of mating behavior may have a genetic basis is suggested."[148]

In addition, the results of this experiment inspired a methodological conclusion:

> The homogeneity of performance found in two highly inbred families emphasizes the value of such animals for studies of sexual behavior. In contrast, the larger interindividual [sic] variance of the heterogeneous animals necessitates the use of very large groups in order to ascertain the role of hormonal and experiential factors which may be contributing to the development of sexual behavior, but whose effect might otherwise be concealed by the differences between animals.[149]

With this insight, Young and his students developed several strains of inbred guinea pigs for further investigations. Like the restriction and isolation experiments discussed by Beach, Young wanted to control experiential factors in order to tease out the

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[148] Valenstein, E., et. al. (1954). "Sex Drive in Genetically Heterogeneous and Highly Inbred Strains of Male Guinea Pigs." Journal of Comparative and Physiological Psychology **47**(2): 162 - 165.

[149] Ibid.

relative of internal versus external factors. Unlike the above-mentioned studies, Young also had the goal of separating the effects of different kinds of internal influences. With the factor of genetic variation under control, they hoped to isolate other factors responsible for the organization of sexual behavior.

In 1955, Young and his colleagues published an article in which they adopted and expanded upon Beach's model. They begin by noting:

> The relative stability of the patterns of sexual behavior displayed by individual male and female mammals has led to speculation and inquiry into the nature of factors that might be responsible for the establishment of such patterns. The possibility that gonadal hormones have an organizing action has long been questioned [by Ball, Beach, and Young himself, among others]. Genetic factors, on the other hand, may be influential. . . . Inasmuch as strains of guinea pigs exist in which the patterns of sexual behavior are relatively homogeneous, these strains seemed well suited for a study that would comprehend not only genetic contribution, but also the possible effect of experience on the development of sexual behavior in a rodent.[150]

The factors that establish these relatively stable patterns are what organize the behavior. Beach had found that rats needed socialization at a critical period in development. With genetic heterogeneity controlled as a factor, Young and his students could further investigate the effects of environment and learning on sexual behavior.

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[150] Valenstein, E., et. al. (1955). "Experiential and Genetic Factors in the Organization of Sexual Behavior in Male Guinea Pigs." Journal of Comparative and Physiological Psychology **48**(5): 397 - 403.

Upon testing the behavior of isolated and socialized males, they found differences in the inbred strains, but not in the heterogeneous control group.[151] Importantly, they made the methodological decision to give specific behaviors different weights. Behaviors leading to "successful" mating (mounting, intromission, ejaculation) were given high weights, while "exploratory" behaviors (sniffling, nuzzling, aborted mounts) were given low weights. There appears to be a teleological motivation to this weighting system: on the assumption that the goal of sexual behavior is pregnancy, those particular behaviors more likely to result in pregnancy are more "successful."[152] In this way, cultural preconceptions influenced methodological analysis.

With this weighting system in place, they found that socialized inbred males exhibited higher levels of heavily weighted behaviors (mounting, intromission, ejaculation). In socialized males from inbred strain 2:

> [T]he difference in the higher measures of sexual behavior (mounting, intromission, ejaculation) are also significant whether the average frequency per animal of the percentage of animals displaying the behavior is considered.[153]

Similarly, in inbred strain 13:

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[151] Valenstein et. al. write:

> The differences in average sexual behavior scores and in the separate measures that contribute to the scores of the isolated and social [heterogeneous] males are not striking. Again, the differences are in favor of the social males, but they are not significant.

Ibid.

[152] (Pointed out by Dennis Des Chene.)

[153] Valenstein, E., et. al. (1955). "Experiential and Genetic Factors in the Organization of Sexual Behavior in Male Guinea Pigs." Journal of Comparative and Physiological Psychology **48**(5): 397 - 403.

> An analysis of the individual measures contributing to the sexual behavior scores reveals that 57 per cent of the social males had intromissions and ejaculations while none of the isolated males exhibited those higher measures of behavior.[154]

In both strains, the isolated males displayed higher levels of less weighted behaviors (sniffling, muzzling, and aborted mounts) and lower levels of the higher weighted behaviors. On the face of it, it would appear that successful mating behavior does require socialization. On the teleological account that informed the weighting system, the socialized males displayed more successful types of behaviors, and thus came closer to the goal of pregnancy.

However, this teleological weighting system carries with it a distinction between quality and quantity. An examination of the quantity of different types of behaviors indicates the need for socialization. But when the authors figured the different weights into their calculations and averaged the scores of each group, they found no significant differences in the weighted averages. The authors explain this lack of difference:

> [B]y the fact that the socially raised males did not exhibit a sufficiently large number of the higher measures of behavior to counter act the greater activity of the isolated males in the lower measures.[155]

In other words, the isolated males made up for their lack of higher weighted behaviors by displaying larger amounts of lower weighted behaviors.

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[154] Ibid.
[155] Ibid.

Young (at this time) interpreted these results as reinforcing Beach's model. The authors conclude the article by claiming that:

> The work with the guinea pig also provides evidence for the existence of dual components of mating behavior, the *organization of the sexual response*, which would correspond roughly to the "capacity for sexual performance" as used by Beach, and *sexual excitability*, which would correspond to "susceptibility to sexual arousal."[156]

From this, the authors conclude that socialization affects the quality, but not the quantity, of sexual behavior. This is a more nuanced claim than Beach's.

The authors noticed one oddity: the performance of the strain 13 males (both isolated and socialized) was significantly below that of the strain 2 and heterogeneous males. The authors postulated that "the deficiency of some substance such as androgen accounted for the poor performance of these males even in the social situation."[157] Presumably, the reasoning behind this claim is that the strain 13 socialized males have had their behavior organized, but they lack sufficient androgens to stimulate said behavior.

To test this hypothesis, the authors castrated thirteen strain 13 males on the day of birth, then injected them daily with 500y of testosterone propionate per 100 gm of body weight (over 20 times the amount sufficient to restore the precastrational level of sexual behavior of adult castrates). Six of the males were isolated, the remaining seven were socialized. After the males reached adulthood, they found that the average behavior

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[156] Ibid.

[157] Ibid.

score of the socialized males was significantly better than both the isolated males and the intact social males from the first experiment.[158]

From the results of these experiments, Valenstein et. al. conclude that:

> The isolated animals gave evidence of being as much aroused by the presence of the female as were those from the social group, and there was no evidence of any emotional disturbance that could have interfered with their display of sexual behavior.[159]

In other words, isolated males were just as susceptible to arousal. To account for this discrepancy between motivation and behavior, the authors claim that the "best explanation of these results appears to be that *the sexual behavior of the isolated animals had not been organized into an effective pattern*."[160] [Original emphasis.]

But what causes successful organization? Is it just learning? On Beach's model, motor patterns and sexual excitability were "innately organized," but successful mating requires socialization. In other words, the organization of adequate sexual behavior

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[158] Ibid.

[159] Ibid. However, these males had difficulty in mating successfully:

> An attempt to improve the performance of the strain 13 males by administering large quantities of exogenous androgen met with only limited success. The performance of the socially raised castrate males receiving androgen was significantly better than that of the untreated males, but it was still significantly below the level of either the strain 2 or the heterogeneous males raised under comparable conditions.

Valenstein, E., et. al. (1955). "Experiential and Genetic Factors in the Organization of Sexual Behavior in Male Guinea Pigs." Journal of Comparative and Physiological Psychology **48**(5): 397 - 403.

[160] Valenstein, E., et. al. (1955). "Experiential and Genetic Factors in the Organization of Sexual Behavior in Male Guinea Pigs." Journal of Comparative and Physiological Psychology **48**(5): 397 - 403.

requires learning (environmental factors), and this learning must take place during a critical period. If animals do not organize their sexual behavior during the critical period, successful matings, regardless of the level of arousal, will not occur.

IV. Questioning the Importance of Critical Periods for Learning

In 1957, Young's group decided to investigate the possibility that isolated males, if given enough later socialization, could mate successfully. In other words, the question was whether early isolation, in and of itself, prevented the display of mature sexual behavior. What inspired this line of inquiry was the earlier finding that isolated males were as active as the socialized males during the tests, although their behavior was limited sniffing, licking, and unsuccessful attempts to mount estrous females (the "lower weighted" behaviors). Instead of an indication that their lack of organization of sexual behavior was a *permanent* state, Valenstein and Goy argue it could be:

> That these lower measures of sexual behavior are in part exploratory, and it was necessary for the isolated males to engage in more of this type of activity before intromission and ejaculation could be achieved. Or, it might have been proposed, that had more tests been given, the full copulatory pattern would eventually have been displayed.[161]

[161] Valenstein, E., and Robert Goy (1957). "Further Studies of the Organization and Display of Sexual Behavior in Male Guinea Pigs." Ibid. **50**(2): 115 - 119.

Contrary to their previous conclusion, the observed lack of success of isolated males could be due to lack of experience *per se*, rather than "to a limited opportunity to organize their sexual behavior."[162] The implicit claim is that Beach conflates environment and learning; that rearing pups in isolation does not mean that they could never learn successful mating techniques. If Beach did indeed make an erroneous conflation, if lack of experience does not result in an inability to learn, then how does sexual behavior become organized? The answer to this question "has a bearing on whether or not we are dealing with a behavior pattern that has an early critical period for its emergence."[163]

Valenstein and Goy conducted five different experiments, which can be divided into two general categories: testing the hypothesis that social isolation, either before or after the critical period, affects mating behavior; and investigating the effects on the organization of sexual behavior of pups raised in non-standard conditions. The first three experiments explored the former, the remaining two the latter.

In the first experiment, Valenstein and Goy tested whether or not a male, which has been able to organize its sexual behavior, displays altered behavior after prolonged isolation. After allowing five pups to mature in group situations, they isolated them for a

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[162] Ibid. Valenstein and Goy note that:

> To support conclusion it was necessary to show that males reared with a minimum of contact with other animals (separation from other members of the litter from time of birth to weaning and complete isolation for designated periods thereafter) were not prevented from displaying the sexual behavior pattern by some effect of the prolonged isolation.

Valenstein, E., and Robert Goy (1957). "Further Studies of the Organization and Display of Sexual Behavior in Male Guinea Pigs." Journal of Comparative and Physiological Psychology **50**(2): 115 - 119.

[163] Valenstein, E., and Robert Goy (1957). "Further Studies of the Organization and Display of Sexual Behavior in Male Guinea Pigs." Journal of Comparative and Physiological Psychology **50**(2): 115 - 119.

period of seven weeks to fourteen months. During this period of isolation, the males were placed with a female on one week to three month intervals. The authors found that isolation did not affect mating behavior, provided that it was already organized.[164] In this way, organization was permanent.

The second experiment tested if mature isolated males, when briefly exposed to test females, are able to organize their sexual behavior. Using three males, each animal was given a series of tests at intervals. As long as the animals remained isolated, they did not display any of the heavier weighted behaviors.[165] These first two experiments support Beach's notion of a critical period.

The third, and ultimately the most important, experiment investigated the question: can a male in which organization of the higher measures of sexual behavior not occurred improve his sexual performance at a more advanced age? To test this, Valenstein and Goy used five males from the heterogeneous stock (including the three from the second experiment) and five from inbred strain 2. While the three were unable to mate with females when briefly exposed, after being placed with females for an extended period of time, "all three demonstrated for the first time the ability to mounts, have intromissions, and ejaculate."[166] The authors took this to imply that, at least for these three males, successful mating behavior could be learned late in life. More evidence for

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[164] Ibid.

[165] Ibid.

[166] Ibid. Perhaps because of their "lack of vigor," inbred strain 13 are never mentioned again by Young's research group. Presumably (and this is only a presumption) they abandoned all research involving strain 13.

this implication came from the remaining two isolated males, who showed distinct improvement after prolonged exposure to females.[167]

In contrast, the five males from inbred strain 2 did not improve as dramatically[168], with the exception of one male. This male, after achieving initially promising results:

> Was then given female cage mates for an additional 25 days, and when retested, he scored 5.8 [a middling score] with several mounts, but still did not have any intromissions or ejaculations. Once again female cage mates were provided, this time for a 30-day period, and three tests were made between days 275 and 295 [of life]. The male's score was raised to 6.6, and now ample evidence was given (two ejaculations and a number of intromissions) of its ability to engage in the complete the copulatory act.[169]

Interestingly, Valenstein and Goy read these results as evidence *for*, not evidence *against*, the idea that sexual behavior could be learned later in life. While the results from the isolated heterogeneous strain tell against Beach's notion of critical periods in development, the results from the inbred strain do not.[170]

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[167] Ibid.

[168] Valenstein and Goy write:

> The results were somewhat different with strain 2 males. In general it was more difficult for them to acquire the copulatory pattern at older ages. . . . Two males were then placed with females for 23 days and retested between days 165 [of life] and 195.

Ibid.

[169] Ibid.

[170] Valenstein and Goy write:

> The remaining three [out of five] strain 2 males were left isolated until day 210 and then retested. None displayed any of the higher measures of sexual behavior. Placed with

The last two experiments investigated the organization of inbred strain 2 male pups' sexual behavior when raised in atypical environments, either an all-male environment or one in which all the females are spayed. (The control group consisted of males raised with intact females.) The goal was "to delimit the type of experiment necessary for the organization of the sexual response."[171] Specifically:

> As estrous females and males initiate mounting whereas untreated, spayed females do not, the importance of mounting as a stimulant to the development of sexual behavior could be determined.[172]

In the fourth experiment, heterogeneous and inbred strain 2 males were paired together, and (to control for higher levels of aggression in strain 2) strain 2 males were caged in groups of two or three. When these males were placed with females, they mated successfully. Because males will occasionally mount other males (an act usually interpreted as dominance behavior)[173] the results from the males raised with other males were not unexpected.

> females for 23 days, they were retested between days 250 and 265. Following these tests they were provided with female cage mates for an additional 30 days and then retested between days 300 and 320. During these tests no mounts, intromissions, or ejaculations were displayed.

Ibid.

[171] Ibid.

[172] Ibid.

[173] Earlier results demonstrated that the acquisition of the copulatory varied with the genetic background of the animals. Specifically, strain 2 males reared with males performed better than those caged with intact females, while heterogeneous animals did not perform so well. The authors postulate that "the strain 2 males may have been aroused by the great amount of mounting that takes place among males caged together." Ibid.

In the sixth experiment, sixteen strain 2 males were each placed with two spayed females, with a control group of ten males placed with intact females. Upon testing, the authors found that:

> The average score of the strain 2 males reared with spayed females is significantly lower than either that of the males which had intact female cages mates or the males caged with males. . . It would appear that, at the time of testing, these males [reared with spayed females] were in the act of acquiring the degree of organization of behavioral necessary, but had not as yet completed the process.[174]

From these experiments, the authors make three conclusions. First, once the copulatory pattern has been organized, prolonged isolation does not affect mating behavior. Second, if the pattern is not organized, the males cannot acquire it upon testing. Both of these conclusions accord with Beach's model. The final conclusion, however, does not.

In contradiction to Beach's conception of critical periods for sexual behavior development, Valenstein and Goy claim that:

> The results from experiments I, II, and II support the conclusion that learning process is involved in the organization of the copulatory behavior pattern of male guinea pigs. It seemed unlikely that males reared with a minimum of contact with other animals were prevented from displaying the full sexual behavior pattern as a direct result of prolonged isolation, but the possibility had not been tested. In the present experiment it was shown that isolation *per se* does not

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[174] Ibid.

> prevent a male from displaying the full sexual pattern provided the behavioral skills had been previously acquired.[175]

In other words, while the organization of mating behavior requires (in part) learning, there does not appear to be a *critical period* for learning sexual behavior. This conclusion is a radical break from both the Beach model and Young's earlier, tentative, suggestion that the organization of sexual behavior has an important genetic component. On the face of it, the empirical results do not support this conclusion. In particular, the first and second experiments confirm Beach's etiological model, while the third is inconclusive at best. Of the five heterogeneous males, the three from the second experiment are unequivocal challenges to Beach's notion of critical periods. However, the authors' claim that the remaining two improved "dramatically" upon repeated testing is questionable.

More problematic is their dismissal of the results from the five inbreds. The fact the five out of ten test subjects confirms a hypothesis, while the other five do not, is still far from conclusive evidence for the authors' thesis. This reflects both the "messiness" of endocrinological research and, relatedly, the power of hypotheses with "thought-experiment" like characteristics. Additionally, granting that the results cast doubt upon Beach's hypothesis, it would appear that, given the dramatic differences between the heterogeneous and inbred strains, these results point to the importance of genetic, rather than environmental, factors on the acquisition of mating behavior.

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[175] Ibid.

Without acknowledging these potential complications, the authors further reinforce their rejection of Beach's notion of critical periods for behavioral development by claiming that:

> The demonstration that organization of the complete copulatory pattern can occur in older animals is of interest. Apparently, this learning process is not restricted to a critical developmental period. To be sure, some of the older males did not organize this pattern.[176]

As such, incongruous results were interpreted as "noise." This glossing over of anomalous results echoes the conclusions of early advocates of the mono-hormonic theory and, more generally, reflects the "messiness" of endocrinological research.

The question about the inequality of potential for sexual behavior, as addressed by Beach and further explored by Young, is a question about the relative influences of external versus internal factors. As such, the debate concerning the etiology of sexual behavior was a debate between two general, intead of elaborated, hypotheses. Young et. al.'s questioning of Beach's notion of critical periods for learning in their 1957 paper set the stage for the crucial resolution of the "problem" of homosexuality.

In conclusion, there are three points of philosophical interest here. First, the rejection of the dominant explanatory model of the etiology of mammalian sexual

[176] Ibid.

behavior is challenged on the basis of one research project.[177] Second, prima facie, experiments 1 and 2 do not support the authors' conclusion that sexual behavior is *not* organized during critical periods of development. If anything, the results from these two experiments reinforce Beach's learning theory. Third, "exceptions to the rule" – older isolated males incapable of organizing a successful mating pattern – do not figure into the general conclusions.[178]

In spite of this, Young and his colleagues used the results of this experiment as a catalyst for a radical new model of the etiology of psychosexual development: the organization/activation model.

V. The Organization/Activation Model

If there is no critical period for the learning of sexual behavior, how does it develop? Two years after the publication of paper questioning the existence of critical periods, Young proposed a radical answer: prenatal exposure to androgens does the organizing. This "organization/activation" model preserves the notion of a critical period, but claims the causal factor to be hormones rather than learning. This model, which is the dominant model of psychosexual development today, is much more

[177] Valenstein and Goy note that "several of the groups contain only a few animals; however, these are believed to be sufficient in view of the unambiguous results and the long period that the animals were followed." Ibid.

[178] This may be a result of Young's decision to focus on homogeneity rather than variability. Nonetheless, this dedication to the typical, at the expense of the atypical, has had serious ramifications. These will be discussed in following chapter.

restrictive in what it considers to be normal or typical masculine or feminine behavior than Beach's model.

Like the work of Frank Lillie and Alfred Jost, investigations into the etiology of sexual behavior make the foundational methodological assumption that one can explain typical development by focusing on atypical development. Underlying this methodological approach is an ontological premise about the difference between typical and atypical development: atypical development is not a part of the normal spectrum of variation, but the result of perturbations in the developmental process. In short, developmental atypicality is pathological. (Though, as we shall see, not all investigators made this assumption.) This assumption immediately raises problems of categorization: what counts as atypical, and why?

As discussed in the previous sections, Young's focus on the relative heterogeneity of behavior suggests that atypicality and typicality can be defined solely in terms of numerical frequency. However, as I demonstrate in the present section, the organization/activation model incorporates prevailing cultural tropes concerning typical and atypical sexual behavior.

In 1959, Charles Phoenix, Robert Goy, Arnold Gerall and William C. Young published "Organizing Action of Prenatally Administered Testosterone Propionate on the Tissues Mediating Mating Behavior in the Guinea Pig," which proposed the organization/activation model of sexual development and behavior. This model suggested that prenatal hormones organize the central nervous system (or "tissues") so that at puberty hormones could activate particular behaviors. Specifically, Phoenix and his colleagues theorized that testosterone primes the male brain, readying it for sex-

related activities such as intercourse and territory defense. The female brain acquires gender[179] in the absence of testosterone.

Adopting Jost's model of female development as the "default" pathway, Phoenix and his colleagues theorized that if femininity were the inherent state, adding testosterone should promote sex-specific neural differentiation in the brain and/or the central nervous system. This sex-specific differentiation would have the effect of permanently fixing an individual's behavior as masculine.

To test this theory, they injected pregnant guinea pigs with testosterone, producing females "in which the external genitalia at the time of birth were indistinguishable macroscopically from those of their male siblings and untreated males,"[180] whom the authors designated 'hermaphrodites'. The authors then performed a series of estrogen and progesterone injections designed to induce estrus, and observed the results. The hermaphrodites (and castrated males) displayed lordosis significantly less

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[179] While the distinction between sex and gender, first proposed by feminist thinkers in the early 1970's, helped clarify discussions of sex-dimorphism in both body and behavior, contemporary endocrinologists (and many psychologists) use these terms interchangeably. Melissa Hines, for instance, writes:

> Some authors try to distinguish between gender differences and sex differences, with gender differences being socially determined and sex differences biologically based. Given our limited knowledge of what is socially or biologically determined, I believe it is impossible to make this distinction. In addition, it is likely that many behavioral sex differences result from complex interactions among different types of influences, some generally considered biological, others social. Finally, the distinction between biological and social influences is in some senses false. All of our behavior is controlled by our brain and, in this sense, is biologically based. For these reasons, the terms *sex difference* and *gender difference* as used in this book will not have different causal implications.

Hines, M. (2004). Brain Gender. New York, Oxford University Press.

[180] Phoenix, C., et. al. (1959). "Organizing Action of Prenatally Administered Testosterone Propionate on the Tissues Mediating Mating Behavior in the Female Guinea Pig." Endocrinology **65**: 369 - 382.

often than the control females. In addition, among the hermaphrodites and castrated males, "the low gutteral growl which is so frequently a part of the pattern of lordosis in normal females, was commonly, and in some individuals always, lacking."[181] The authors also determined that the larger the quantity of androgens injected prenatally, the greater the suppression of lordosis.

What made Phoenix et. al.'s 1959 paper special was not the results (which had been uncovered earlier), but their explanations of the results. Previous researchers had noticed an increased responsiveness of masculinized rodents to doses of androgens in adulthood, but had explained this as a manifestation of an inherent bisexuality. In contrast, Phoenix et. al. theorized that prenatal hormones organized the neural tissue in "the direction of masculinization or feminization."[182] Gonadal hormones secreted in adulthood "activate" the previously organized tissues to induce masculine or feminine behavior.

Importantly, the authors considered their findings to be an extension of the work done by Jost on the differentiation of the genital tracts. They interpreted Jost's work as demonstrating an "inequality in potential": while prenatal exposure to androgens will only slightly affect male genital development, it has a profound effect on female development.[183]

Phoenix et. al. concluded that the altered behavior of the hermaphrodites demonstrated that testosterone "acts on the central nervous tissues in which patterns of

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[181] Ibid.

[182] Ibid.

[183] Ibid.

sexual behavior are organized."[184] The authors acknowledged the widespread existence of bisexual behavior, but downplayed its importance. While untreated females in the experiments occasionally mounted other rats, and untreated males occasionally displayed lordosis, this behavior did not figure into their explanations. For instance, in their 1957 paper, two of Young's colleagues speculated that mounting behavior stimulated the learning process in young males. To explain their reasoning for placing some young males with spayed females and others with intact females, the authors point out that as:

> Estrous females and males initiate mounting whereas untreated, spayed females do not, the importance of mounting as a stimulant to the development of sexual behavior could be determined.[185]

However, the authors express no interest in investigating the causes of female mounting. Indeed, the authors reinterpret previous results in light of the organization/activation model, pointing out that earlier researchers, with their assumption of potential bisexuality, had failed to explain properly the masculinized behavior of androgen-treated animals:

> The possibility that there might have been a suppression of the capacity to respond as females and therefore an inequality of potential does not seem to have

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[184] Ibid.

[185] Valenstein, E., and Robert Goy (1957). "Further Studies of the Organization and Display of Sexual Behavior in Male Guinea Pigs." Journal of Comparative and Physiological Psychology **50**(2): 115 - 119.

> been considered. . . We suggest, however, that in the adult this bisexuality is unequal in the neural tissues as it is in the case of the genital tissues.[186]

This extends the default model from physical to neural development and, ultimately, behavior. The notion that there is an "inequality in potential" has fueled a host of studies trying to determine the relationship between not just hormones and behavior, but also hormones and intellectual capacities.

Building upon the work of Lillie and Jost, the general explanatory mechanism of sex differences is as follows: The presence of a Y chromosome initiates a chain of events that causes primitive fetal gonads to develop into testes (without the Y chromosome, the fetus develops as a female). The testes begin secreting androgens, which cause structural changes in both the genitalia and the brain. The sex differences in brain structure underlie sex differences in behavior and cognitive abilities. This general explanatory model serves to explain not just normal physical and behavioral development (including sex differences in aggression and cognitive abilities), but also the emergence of homosexuality, transsexualism, and gender-atypical behavior correlated with endocrine abnormalities. This general explanatory mechanism is the foundation for current theories of human gendered behavior.

There are four points of interest with this paper. First, the authors only present positive arguments; there is no discussion of the deficits of Beach's model. On the face of it, it appears the Young and his students have dismissed Beach's model out of hand. Second, the model itself influences how the data are interpreted. For instance, the

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[186] Phoenix, C., et. al. (1959). "Organizing Action of Prenatally Administered Testosterone Propionate on the Tissues Mediating Mating Behavior in the Female Guinea Pig." Endocrinology **65**: 369 - 382.

masculine behavior of untreated adult females is considered "noise." Third, the organization/activation model does not require the mono-hormonic hypothesis. While building upon the Jost paradigm, mono-hormonism is not necessary for the organization/activation model. Neural tissues could be organized by both estrogens and androgens (as, in fact, they are).[187] This reflects the power of crucial resolutions and how they shape the development of a field. Finally, past results were reinterpreted in light of the model, implying that a field's *past* is also reformed upon the acceptance of a new model.

By the mid 1960's the organization/activation model was widely accepted, not just in the field of endocrinology,[188] but in other scientific fields as well, including psychology. One of the authors of the 1959 paper, William C. Young, enthusiastically emphasized the potentially broad impact of the organization/activation hypothesis. If, as he predicted, prenatal hormones influenced a wide variety of behaviors, adopting the organization/activation hypothesis would unite:

> [T]he work of experimental embryologists who have concerned themselves so completely with all that is involved in the development and differentiation of the genital tracts, and the work of psychologists and psychiatrists for whom the

[187] See, for instance, Toran-Allerand, C. D. (1981). "Gonadal Steroids and Brain Development: In Vitro Veritas?" Trends in Neurosciences **4**: 118 - 121.

[188] See, for instance, Lehrman, D. (1961). Gonadal Hormones and Parental Behavior in Birds and InfraHuman Mammals. Sex and Internal Secretions. W. Young. Baltimore, The Williams and Williams Company. **III:** 1268-1383.; Whalen, R. (1991). Heterotypical Behaviour in Man and Animals: Concepts and Strategies. Heterotypical Behaviour in Man and Animals. B. a. A. Haug. London, Chapman and Hall.

> development and differentiation of neural tissues presents problems of equal interest and importance.[189]

Human behavior, once strictly the province of psychology, came under the rubric of behavioral endocrinology.

The organization/activation model provided (and still provides, as I show later) the impetus to search for the neurological basis of sexually dimorphic behavior – not merely the brain structures underlying the positive feedback loop that supports ovulation, but also sexual orientation and, eventually, gender identity. To put this in more philosophical terms, the organization/activation model inspired many scientists to embrace a new framework for developing hypotheses. In Lakotos's sense, it became a new research program.

This widespread acceptance coincided with a decrease in the importance attributed to individual genetic variation, environmental cues and learning in the development of sexual behaviors.[190] For example, early on in the history of behavioral endocrinology, researchers noticed that lab animals varied widely in their levels of sexual activity. More interestingly, most males, after being castrated and then treated with

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[189] Young, W. C. (1961). The Hormones and Mating Behavior. Sex and Internal Secretions. W. C. Young. Baltimore, The Williams and Wilkins Company. **II**.

[190] Slijper, in his concluding remarks of his 1984 article criticizing the work of Ehrhardt and Meyer-Bahlburg, notes that:

> Although it is impossible to separate the influence of androgen hormones from that of psychosocial factors on behavior, most studies have not even considered environmental influences.

Slijper, F. (1984). "Androgens and Gender Role Behaviour in Girls with Congenital Adrenal Hyperplasia (CAH)." Progress in Brain Research **61**: 417 - 422.

testosterone replacement therapy, eventually returned to their earlier activity levels, regardless of the amount of testosterone given.[191] Beach had attributed these variations in behavior to individual differences in temperament and learning as well as to different hormone levels. After the introduction of the organization/activation theory, these variations were explained as due to different levels of prenatal androgens: after the brain had been organized in a certain way, later injections of androgens would simply activate the brain to cause certain behavior, no matter what the dose (so long as it was above a certain threshold level). William C. Young, one of the authors of the 1959 paper, claims that this particular reaction to testosterone:

> [C]ould be likened to an exposed but undeveloped photographic film or plate, the hormone to the developer. The pattern of behavior or "picture" that would be brought out by the hormone would depend on what had been taken; with this the character of the soma [somatic or constitutional factors] was held to be analogous.[192]

Few scientists mentioned that prenatally "ordered" males still needed postnatal organization through social contact in order to display adequate mating behavior.[193] As a

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[191] Young, W. C. (1961). The Hormones and Mating Behavior. Sex and Internal Secretions. W. C. Young. Baltimore, The Williams and Wilkins Company. **II**.

[192] Ibid.

[193] Earlier findings demonstrated that male rats needed social contact in order to learn how to mate properly. For a summary and further investigation, see Hard, E., and Larsson, Knut (1968). "Dependence of Adult Mating Behavior in Male Rats on the Presence of Littermates in Infancy." Brain, Behavior and Evolution **1**(5): 405-419.

result, male and female rodent behaviors emerged as more stereotyped than they had previously seemed, and more rigidly determined by prenatal hormone exposure.[194]

Sex differences in the brain have long been accepted as providing the underlying neurological structure supporting ovulatory competence. But ovulatory competence, gender identity, and sexual orientation are, on the face of it, radically different phenomena. As will be discussed in detail in chapter seven, an explanatory schema that explains phenomena previously thought to be dispirit is a hallmark of unification.

This general model of psychosexual development serves as the basis of research in behavioral endocrinology to this day. For example, in his review of male psychosexual development, Dick Swaab writes:

> Sexual differentiation of the brain is thought to be 'imprinted' or 'organized' by hormonal signals from the developing male gonads. . . . Male sexual differentiation of the human brain is thought to be determined in the first two periods during which sexually dimorphic peaks in gonadal hormone levels are found – during gestation and the perinatal period, while from puberty onwards, sex hormones alter the function of previously organized neuronal systems ('activating effects').[195]

[194] Beach continued to challenge the organization/activation thesis, although his criticism fell on mostly deaf ears. See "get name of article" in *Proceedings of the National Academy of Science*, 1966, p. 532.

[195] Swaab, D. (2004). "Sexual Differentiation of the Human Brain: Relevance for Gender Identity, Transsexualism and Sexual Orientation." Gynecological Endocrinology **19**: 301-312.

Part of the reason for this rapid and continued widespread acceptance was the unifying explanatory promise of the model. In "Sexual Differentiation of the Vertebrate Brain: Principles and Mechanisms," Cooke et al. write:

> Perhaps the most important contribution of the organizational hypothesis was to draw attention to the question of why males and females behave differently. After this landmark paper [1959] the question was refined to, "what is different about males and females that causes them to behave differently?" Once this question was posed, the most obvious potential answer was that the brains of males and females were structurally different.[196]

Delineating one causal factor behind the developmental pathway – hormones – streamlines the explanatory model.

Another reason for the rapid acceptance of the organization/activation model is given by Professor Jacob van der Werff ten Bosch, an endocrinologist at Erasmus University in Rotterdam who conducted research on hormones and brain development in the 1960s: the organization/activation model provided a possible solution to the "vexing question of homosexuality."[197]

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[196] In "Sexual Differentiation of the Vertebrate Brain: Principles and Mechanisms," Cooke et. al., claim:

Cooke, B., et. al. (1998). "Sexual Differentiation of the Vertebrate Brain: Principles and Mechanisms." Frontiers in Neuroendocrinology **19**: 323 - 362.

[197] From an interview by the author in van den Wijngaard, M. (1997). Reinventing the Sexes: The Biomedical Construction of Femininity and Masculinity. Bloomington, Indianna University Press. In *Sexing the Body*, Anne Fausto-Sterling claims three factors contributed to the rapid acceptance of the organization/activation model: it built on Jost's already accepted accounts of anatomical development; it had an apparent widespread applicability; and it focused on the

The two explanations mentioned for the widespread and rapid acceptance of the organization/activation model are not incompatible. Whatever their particular reasons, scientists not only accepted the model without the same sort of caution that initially characterized the reception of Jost's ideas, they quickly extended the organization/activation model to other "gendered" behaviors, including maternal care, aggression, activity level, play fighting, maze learning, and taste preference.

VI. Challenges to the Organization/Activation Model

The main challenge to the organization/activation hypothesis was the discovery in the mid-1960's that early estrogen treatment can masculinize the central nervous system. Specifically, a single injection of estradiol, when given to newborn male rats that had been castrated *in utero*, drastically masculinized their behavior.[198]

This discovery challenged the organization/activation hypothesis on two fronts. First, and most generally, it raises the question of how an ovarian steroid can cause masculinization. The fact that it can do so threatens the mono-hormonic theory of sexual development for both body and brain; that it is the androgens, and only the androgens,

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socially acceptable heterosexual development. Fausto-Sterling, A. (2000). Sexing the Body. New York, Basic Books.

[198] Feder, H., and Richard Whalen (1965). "Feminine Behavior in Neonatally Castrated and Estrogen-Treated Male Rats." Science **147**(3655): 306 - 307. The authors did not interpret their results as discrediting the organization/activation hypothesis, but as confirming the mono-hormonic theory of development: "feminization is induced by lack of neonatal androgen rather than by the presence of estrogen." Feder, H., and Richard Whalen (1965). "Feminine Behavior in Neonatally Castrated and Estrogen-Treated Male Rats." Science **147**(3655): 306 - 307.

that organize. The second question raised is more specific: why doesn't estradiol from the newborn female's ovaries (or from the mother while *in utero*) masculinize the females?

To preserve the organization/activation hypothesis, two groups of researchers proposed the "aromatization" hypothesis. In 1970, a group of scientists at the Royal Veterinary College in London discovered that a metabolite of testosterone that cannot be aromatized into estradiol did not stimulate copulatory behavior in rats.[199] They speculated that the influence of androgens upon sexual behavior depended upon their metabolic conversion to an estrogen. Because testosterone and estradiol are structurally similar, a single chemical reaction can convert testosterone to estradiol.[200] This type of process is known as "aromatization," and is facilitated by the enzyme aromatase. Thus, tissues containing aromatase can convert testosterone to estradiol and thereby make use of estrogen receptors.

Two years later, a group of researchers at the University of California at San Diego discovered that the developing human brain itself is a site of aromatization.[201] This prompted them to "look for the presence of the same system in the central nervous

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[199] McDonald, P., et. al. (1970). "Failure of 5-alpha-dihydrotestosterone to Initiate Sexual Behavior in the Castrated Rat." Nature **227**: 964 - 965.

[200] The substitution of a hydroxy-group for a double-bonded oxygen while, at the same time, losing both a hydrogen atom and a methyl group.

[201] Naftolin, F., et. al. (1971). "Aromatization of Androstendione by Limbic System Tissue from Human Foetuses." Journal of Endocrinology **51**(4): 795 - 796.

system and anterior pituitary gland of adult male and female rats,"[202] which they subsequently found.[203]

Combining the chemical and behavioral findings, these two groups of researchers theorized that it is *estradiol* that masculinizes the brain, not testosterone. Systemic testosterone could be converted to estradiol and stimulate estrogen receptors in the hypothalamus. This was why injections of estradiol to newborn females could masculinize their behavior.

The aromatization hypothesis was bolstered by later studies finding the same system of conversion in the hypothalmi of young and fetal rats.[204] The subsequent observation that injecting neonatal female rats with an estrogen antagonist blocked the effects of testosterone treatment provided additional support. Specifically, blocking the aromatization process or blocking estradiol receptors during early development prevented the development of male-typical behavior patterns.[205]

This answers the general question, but not the specific one: how do females escape masculinization? While the ovaries of fetuses and newborns secrete very little

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[202] Naftolin, F., et. al. (1972). "Aromatization of Androstenedione by the Anterior Hypothalmus of Adult Male and Female Rats." Endocrinology **90**(1): 295 - 298.

[203] Naftolin and McLusky discovered aromatase in the adult rat hypothalamus, For a summary, see MacLusky, N., and Naftolin, Frederick (1984). Aromatization Hypothesis. Differentiation: Basic and Clinical Aspects. Reddy et. al. discovered it in newborns: Reddy, V. V. R., et. al. (1974). "Conversion of Androstenedione to Estrone by Neural Tissues from Fetal and Neonatal Rats." Endocrinology **94**(1): 117 - 121. See also Baum, M. (1979). "Differentiation of Coital Behavior in Mammals: a Comparative Analysis." Neuroscience and Biobehavioral Reviews **3**(4): 265 - 284.

[204] Reddy, V. V. R., et. al. (1974). "Conversion of Androstenedione to Estrone by Neural Tissues from Fetal and Neonatal Rats." Endocrinology **94**(1): 117 - 121.

[205] Doughty, C. (1975). "Inhibition, by Anti-Estrogen MER-25, of Defeminization." Journal of Endocrinology **67**: 459 - 460.

hormone, all fetuses are exposed to fairly high levels of estrogens produced by the mother's ovaries during pregnancy. Thus it would appear that, not only should females be masculinized, they should be more masculinized than their male womb-mates. In other words, the aromatization hypothesis, while resolving one anomaly, raised another.

The solution is a protein (called the 'α-feto protein') in the blood of rat fetuses. Found in both sexes, this protein binds estradiol from both the mother and fetal ovaries, but not testosterone, thus limiting the developing brain's exposure to estradiol. The developing yolk sac and fetal liver synthesize this protein, which circulates at high concentrations during the latter part of gestation and then gradually disappears over the first few weeks of postnatal life.[206] But the testosterone secreted by the male fetuses is *not* bound by the α-feto protein. This testosterone enters the brain cells, beyond the reach of the binding protein, and is locally aromatized to estradiol. The estradiol triggers (via estrogen receptors) some cascade of neural events that inhibits the expression of ovulation and lordosis.[207]

The aromatization thesis rescues the hypothesis that prenatal androgens organize the brain (even if it is, technically, an estrogen that does the organizing). But the aromatization thesis, unlike the organization/activation model, was initially resisted by the scientific community. Richard Whalen, in 1974, writes:

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[206] Plapinger, L., et. al. (1973). "Ontogeny of Estradiol-Binding Sites in the Rat Brain." Endocrinology **93**(5): 1129 - 1139.

[207] McEwen, B. S., et. al. (1975). "Role of Fetoneonatal Estrogen Binding Proteins in the Associations of Estrogen with Neonatal Brain Cell Nuclear Receptors." Brain Research **96**(2): 400 - 406.

> This hypothesis is intriguing because it has been known since our early work that the administration of estrogen to newborn female rats will work like testosterone to inhibit the later display of lordosis behavior . . . Of course, these findings in no way prove that sexual differentiation is controlled by an estrogen. The data are cited to raise the critical issue of the role of steroid metabolism in the differentiation process.[208]

Other scientists described aromatization as a process whereby estrogens *mimic* androgens. One textbook author theorizes that:

> Since both types of steroid hormone [estrogens and androgens] inhibit gonadotrophin secretion, one hypothesis states that it is not action of the steroid [estradiol] directly, but the suppression of gonadotrophin secretion at a critical stage, which affects the hypothalamus.[209]

It took several years for scientists to accept the aromatization hypothesis. Roger Gorski, initially resistant to the hypothesis, appears to have accepted it by 1979: "we have the seemingly unusual situation where estradiol appears to be the vehicle for

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[208] Whalen, R. (1974). Sexual Differentiation: Models, Methods and Mechanisms. Sex Differences in Behavior. R. Friedman, and van de Wiele. New York, Kruger.

[209] Martin, C. (1976). Textbook of Endocrine Physiology. Baltimore, The Williams and Wilkins Company. Almost twenty years later, in their review of sex differences in the human hypothalamus, Swaab and Hofman write:

> The presence of aromatase in the developing brain explains the extraordinary ability of oestrogens to mimic, at least partly, the organizing actions of androgens.

Swaab, D., and Hofman, Michel (1995). "Sexual Differentiation of the Human Hypothalamus in Relation to Gender and Sexual Orientation." Trends in Neurosciences **18**(6): 264 - 270.

masculinization of the brain."[210] It is now generally accepted that "though it may be counterintuitive that a female hormone is ultimately responsible for development of the male brain, the data reported thus far demonstrate that such is the case."[211] This initial resistance may be due to cultural preconceptions about differing inducing factors. (See my earlier comments about the initial gendering of hormones.)

But the aromatization hypothesis did not solve all the challenges raised by the theory that estradiol masculinizes the brain. Recall that the general challenge to the organization/activation model was resolved by the aromatization thesis, while the discovery of the α-feto protein resolved the specific one. The aromatization thesis appeared to uphold the essence of the idea that androgens are responsible for masculine brain differentiation. But later research cast these solutions into doubt. Testosterone aromatization, thought to be responsible for dimorphism in the rat brain, does not occur in primates. Specifically, scientists soon discovered that the equivalent of α-feto protein in primates did not bind estradiol, or at least bound it inefficiently.[212]

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[210] Gorski, R. A. (1979). "The Neuroendocrinology of Reproduction: An Overview." Biology of Reproduction **20**(1): 111 - 127.

[211] Schulkin, J. (1999). The Neuroendocrine Regulation of Behavior. New York, Cambridge University Press.

[212] MacLusky and Naftolin note that

> There is no a priori reason to suppose that aromatization does not play a part in the response of the developing human or guinea pig CNS to prenatal androgen. Yet, in both man and guinea pig, we apparently cannot invoke α-fetoprotein as a mechanism for the regulation of free circulating estrogen levels during gestation.

MacLusky, N. J., and Naftolin, Frederick (1981). "Sexual Differentiation of the Central Nervous System." Science **211**(4488): 1294 - 1303.

There are basically two solutions to this challenge to the aromatization hypothesis. The first is an invocation of a version of the di-hormonic theory: androgens, as well as estrogens, act directly on the brain. Simon LeVay, for instance, claims that "testosterone's effects do not requires this conversion [to estradiol]" in primates.[213] Although generally accepted by the scientific community, the exact mechanisms behind this updated version of the di-hormonic remain elusive. In their study of interactions between gonadal hormones and gene expression, van Nas et. al. write:

> The organizational and activational effects of testosterone may be mediated by two primary metabolites of testosterone: nonaromatized metabolites such as dihydrotestosterone (DHT), which bind to androgen receptors, and aromatized metabolites such as estradiol (E2), which bind to estrogen receptors.[214]

The second solution is to postulate that the primate placenta protects the developing fetus from maternal estrogens by rapidly metabolizing them. Specifically, some endocrinologists surmise that the placenta converts estradiol to the much weaker hormone, estrone.[215] In both cases, the organization/activation model remains firmly in place as the dominant model in theories of psycho-sexual differentiation.

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[213] LeVay, S. (1993). The Sexual Brain. Cambridge, The MIT Press.

[214] van Nas, A., et. al. (2009). "Elucidating the Role of Gonadal Hormones in Sexually Dimorphic Gene Coexpression Networks." Endocrinology **150**(3): 1235 - 1249.

[215] In his extensive review of research on the etiology of homosexuality, Heino Meyer-Bahlburg writes:

> Endogenous estradiol is believed to be largely inactivated before it reaches the fetal brain, in rats by binding to alpha-fetoprotein, in the rhesus monkey and, possibly, in man by placental conversion to the relatively ineffective estrone.

VII. Conclusion

Beach's notion of organization set the conceptual framework for the succeeding organization/activation model, but with the "organization" due to prenatal hormones, not early learning. This shift in emphasis to prenatal hormones had several effects on the field of endocrinology.

First, it reinforced the mono-hormonic model of development, and extended it from physical to behavioral development. The initial resistance to the role of estrogens, and later interpretation of of that role in terms of the mono-hormonic theory, indicates the extent of this reinforcement. This is in spite of the fact that mono-hormonism is not necessary for the organization/activation model: an underlying assumption of the di-hormonic theory could support the model just as well. Second, "typical" male and female development came to be seen in a more dichotomous fashion, as opposed to the "continuum" approach of Beach. This rejection of bisexuality (in the general sense) is logically incidental, but had tremendous social and scientific consequences, as will be discussed in the following chapter.

More broadly, the history discussed in this chapter sheds light on the processes of determining factors. In particular, initial hypotheses concerning causal factors occasionally must be refined to account for temporal points in development. The

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Meyer-Bahlburg, H. (1984). "Psychoendocrine Research on Sexual Orientation: Current Status and Future Options." Progress in Brain Research **61**: 375 - 398. See also Jensen, E., and Eugene DeSombre (1973). "Estrogen Receptor Interaction: Estrogenic Hormones Effect Transformation of Specific Receptor Proteins to a Biochemically functional Form." Science **182**(4108): 126 - 134.

investigations into early learning experience revealed the important of both proximal causes (such as giving pregnancy and giving birth instigating nest-building) and distal causes (such as learning to pick up and carry materials as developing the capacities necessary for nest-building). More dramatically (in terms of the development of the field) the basic innovation of the organization/activation model was to push the critical influence of hormones back from adulthood to embryonic development.

Finally, the history discussed demonstrates the power of crucial resolutions. The crucial resolution of the freemartin problem lead to the adoption of mono-hormonism, a conception of development adopted by the organization/activation model, even though it was not necessary. As discussed in the next chapter, the resolution of the "problem" of homosexuality was crucial, in that it was the deciding factor between two general theories of sexual development (Beach's versus the organization/activation model).

The organization/activation model promised to extend the Jostian model of physical sexual development to the brain and, ultimately, behavior. Because this model serves to explain not just normal physical and behavioral development, but also pathological development, it was rapidly adopted by the scientific community. As the theoretical foundation for contemporary behavioral endocrinology, scientists (including not just endocrinologists but psychologists and the medical community in general) consider the model applicable to humans as well as laboratory animals.

As I discuss in the next chapter, the acceptance of the organization/activation model was not because it solved a number of persistent anomalies. Instead, it was rapidly accepted by the majority of the scientific community, in part, because it provided the groundwork for a crucial resolution of *one* persistent "anomaly," that of homosexuality.

But the rapid acceptance of this model is also due to a more general factor: the appeal of explanatory unification. I explore this in chapter six.

Chapter 5

The "Problem" of Homosexuality

I. Introduction

Until the advent of the organization/activation model, the primary model of the etiology of sexual behavior was due to Frank Beach. As a result, scientists in general (and the medical community in particular) were faced with one of two choices: accept homosexuality as a normal variation within the spectrum of behavior; or regard it as pathological, even though no satisfactory biological model existed able to explain the pathological aspects of homosexuality.

For those researchers who considered homosexuality to be a pathology,[216] two elaborated hypotheses were available. One hypothesis posited early psychological experience as the causal agent, which, in emphasizing environmental factors, presumes that mammals are undifferentiated at birth in terms of capacity to exhibit sexual behaviors. The other hypothesis claimed that homosexuality was due to persistent hormonal imbalances in adulthood. In emphasizing biological factors, this second

[216] It should be noted that there was, within the field, a minority but influential view that did *not* consider homosexuality (and transsexuality) to be pathological, most notably that of Frank Beach and, as I discuss in the tenth chapter, Harry Benjamin.

hypothesis presumes that mammals are differentiated inherently in terms of sexual behavior (and thus sex-atypical behavior is a pathology).

Much like Lillie's resolution of the freemartin problem, the resolution of the "vexing problem of homosexuality"[217] was crucial. It made possible a resolution to the more general controversy concerning the etiology of sexual behavior, was formulated in advance of convincing empirical experiments (and thus took on the character of a thought experiment), and inspired a research program dedicated to uncovering the mechanisms responsible for specific developmental outcomes. I address this issue in detail in this and following chapters.

In what follows, I detail the early hypotheses of the etiology of homosexuality, as well as how the organization/activation model provides a crucial resolution to the "problem" of homosexuality. Finally, I present a research program dedicated to providing empirical confirmation of this resolution.

II. Early Hypotheses

Early endocrinological studies did not distinguish between homosexuality, hermaphroditism, and tranvestitism. This is in part due to the lack of information about the relative influences of hormonal, genetic, and environmental contributions of phenotypic and behavioral outcomes. In their 1942 review, Witschi and Mengert note

[217] Professor Jacob van def Werff ten Bosch, an endocrinologist at Erasmus University in Rotterdam, quoted in van den Wijngaard, M. (1997). Reinventing the Sexes: The Biomedical Construction of Femininity and Masculinity. Bloomington, Indianna University Press.

that the study of human hermaphrodites (what they also call "sex-reversed" individuals) raises the question:

> [A]s to what extent homosexuality may rest upon sex reversal. That a large proportion of homosexuals is of a purely environmental type is clearly brought out by studies like the most recent one by Henry. However, indications of the existence of a congenital and probably hereditary type are numerous.[218]

This parsing of internal versus external causal factors in terms of environment versus "heredity" (genes) reflects the early, and eventually abandoned, emphasis upon the genetic factors underlying the etiology of sexual behavior.[219]

More fundamental to the discussion of the etiology of homosexuality than the relative influence of internal versus external factors is that of typicality (or normality) as opposed to atypicality (or abnormality). Albert Ellis, in his 1945 review of the literature on hermaphroditism in English, begins by pointing out that:

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[218] Witschi, E., and Mengert, William (1942). "Endocrine Studies on Human Hermaphrodites and Their Bearing on the Interpretation of Homosexuality." Journal of Clinical Endocrinology **2**(5): 279-286.

[219] In spite of their emphasis upon the possible genetic factors behind homosexuality, Witschi and Mengert conclude their study by noting that:

> We had become accustomed to look at human sex determination as a solved problem, as a toss-up between X and Y chromosomes. Deviations of sex ratio, and of morphological and endocrine physiology, as well as of behavior, were only considered oddities. Now as matters of sex are no longer shrouded with deep secrecy, we begin to realize that aberrations due to modifying genes and special hormonal conditions are much more prevalent than ever suspected.

Ibid.

> In the field of human sexuality, there are two major domains, the so-called "normal" and "abnormal," in neither of which, as yet, we have definitive answers to even a fraction of the vitally important recurring behavioral question. Thus, regarding the matter of homosexuality, there have been, and are still, two opposed viewpoints concerning its origins. The orthodox sexological view has been that sexual inversion is "constitutionally" rooted: and that homosexuals are born, not conditioned; and that hormonal or/and genic imbalances cause homosexuality. Quite opposed to this view of homosexuality has been that which insists that the main etiological factors in homosexuality are psychogenic rather than genic.[220]

This "orthodox" view was held by many early endocrinologists, including such luminaries as Richard Krafft-Ebing (the first person to write about homosexuality in medical terms) and Magnus Hirschfeld (a medical doctor who championed the rights of homosexuals).

Researchers investigating the orthodox view looked to human hermaphrodites to deduce the genetic and/or hormonal causes of homosexuality. While this research plan appears dubious to contemporary eyes, Albert Ellis explains the reasoning behind it as follows:

> [W]hether human hermaphroditism is fundamentally caused by direct genetic factors or by hormonal imbalances (which may themselves be genetically caused),

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[220] Ellis, A. (1945). "The Sexual Psychology of Human Hermaphrodites." Psychosomatic Medicine **7**(2): 108 - 123. A later commentator writes:

> It is noteworthy that Havelock Ellis (1933) stressed the importance of constitutional factors, and, on the analogy of the intermediate sexual types produced by breeding moths of different species together, regarded homosexuality as a variety of hermaphroditism.

Neustatter, W. L. (1954). "Homosexuality: The Medical Aspect." The Practitioner **172**(1): 364 - 373.

there seems little doubt that it is a somatic anomaly with deep physiological roots. The crucial question therefore arises: should not the same physiological factors which disturbed the soma of the hermaphrodite so drastically, equally affect his or her psyche? If, as has been contended by many reputable geneticists, biologists, and psychiatrists, the direction of the human sex drive depends primarily on hormonal or genetic factors; if homosexuality actually is rooted in physiological rather than psychogenic influences, would it not then be reasonable to expect heavily masculinized hermaphrodites usually or invariably to have masculine libidos and very feminized ones to have feminine libidos.[221]

Contrary to this expectation:

[T]here is nothing in our data to indicate that there is a significant difference between the amount of sexual deviation – homosexuality, bisexuality, and psychosexual immaturity – to be found among these hermaphrodites and among a presumably representative group of non-hermaphrodites.[222]

Thus implying the link between hermaphroditism and homosexuality to be tenuous at best. (Also implying a disconnect between physical and psychological development.) Eventually, they came to be regarded as two distinct phenomena.

[221] Ellis, A. (1945). "The Sexual Psychology of Human Hermaphrodites." Psychosomatic Medicine **7**(2): 108 - 123.

[222] Ibid.

Because the field of genetics was in its infancy,[223] researchers subscribing to the orthodox view shifted their focus to hormones. As such, the working hypothesis was that homosexuality was the result of persistent hormonal imbalances.

Even as the field of genetics progressed, many researchers were hesitant to invoke genetics as the (sole) cause of homosexuality, while still postulating an (as yet unknown) biological factor:

> Many regard the excess of male [as opposed to female] deviants as evidence of the operation of a biological factor . . . Other workers point to the universal identification of the young child with its mother. In the female the mother model remains of prime importance, but the male child must turn towards his father as a model for later behaviour. Genetic studies have been inconclusive, for while F. J. Kallman observed a 100% concordance rate for homosexuality between monozygotic twins others have cast doubt on his observations. Chromosomal sex always corresponds to anatomical sex and in fact no abnormalities of the chromosomes have been detected in this condition. At present no clear-cut genetic hypothesis is tenable, and it seems unlikely that inborn errors can ever provide a complete explanation of this disorder.[224]

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[223] In his review of intersexual (hermaphroditic) development, Goldschmidt points out:

> In vertebrates we do not know anything about the primary sex-determining stuffs, produced by the sex-genes; but certainly [about] the secondary determining substances . . . whether they are identical with the sex-hormones *sensu stricto* or not.

Goldschmidt, R. (1938). "Intersexuality and Development." American Naturalist **72**(740): 228 - 242.

[224] (1965). "Origins of Homosexuality." British Medical Journal **2**(5470): 1077-1078.

Unfortunately, the orthodox view did not have unambiguous empirical support.[225] This is in part because the laboratory techniques and chemical understanding at this time were simply too primitive to provide a convincing case. With the gradual improvement in the accuracy and sensitivity of chemical assays, the initial hypothesis of endocrine imbalance became more and more dubious. For instance, Robert Laidlaw writes:

> Coming now to the causes of homosexuality, I can assure you that this is a very muddy and debatable field. . . . Is this homosexual phenomenon something which is psychogenic, or is it something which comes from environmental conditioning? Or is it something which is inherent, constitutional in the individual? Or is it something which goes even further back into hereditary trends?[226]

In other words, is the (presumably singular)[227] phenomenon of homosexuality due to what we would now loosely call mental illness, learning, hormonal factors, or genetics? Or, as Laidlaw puts it:

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[225] Hooker, in his review, notes that "attempts to relate homosexual behavior to sex hormones have not been uniformly successful." For example:

> In one series of four eunuchoid homosexual males the administration of testosterone propionate converted all into normal males. In another series of eleven, however, only three reported benefit, while five reported intensification of their homosexual drive under treatment with testosterone and chorionic gonadotrophin.

Hooker, C. W. (1946). "Reproduction." Annual Review of Physiology **8**: 467 - 495.

[226] Laidlaw, R. (1952). "A Clinical Approach to Homosexuality." Marriage and Family Living **14**(1): 39 - 46.

[227] It is interesting to note that Laidlaw, while assuming there to be multiple causes contributing to homosexuality, nonetheless treats it as a unitary phenomenon in his review, in spite of his earlier acknowledgment that:

> It would be so much easier (as Kinsey points out), in a search for causative factors, if we were looking for factors which would cause a total heterosexual pattern or a total

> How much weight should we lend to hereditary and constitutional factors in the creation of the homosexual, as opposed to environmental and developmental factors? I can assure you that this is a subject which is far from settled at the present time, and in the literature we find again a continuum where, at the one pole, Hirschfield feels that every homosexual is constitutionally predetermined, and going to Havelock Ellis, who feels that, although there is such a predisposition, there is more of an environmental factor – and then going on to Freud and to Brill and to Stekel, who progressively lay greater and greater stress upon environmental factors.[228]

Because of the clinical failures to uncover hormonal imbalances (discussed in more detail later), the prevailing, *general* hypothesis invoked 'psychogenic' factors. Accordingly, homosexuality is the result of external, environmental factors, rather than internal, 'constitutional' factors.[229]

Those psychologists investigating the causes of homosexuality, for the most part, tended to appeal to psychoanalytic explanations; a tend understandable due to the fact that Freudian-inspired theories of psychosexual development were the prevailing general explanatory model within the field. For instance, in his review of the medical aspects of

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> homosexual pattern. But where we are seeking for causes that will explain this continuum [Kinsey's continuum of sexual behavior] going all the way from one pole to another, we are up against a very involved problem.

Ibid.

[228] Ibid.

[229] Albert Ellis, commenting on Laidlaw's paper, claims "at least ninety percent of recent authorities would agree that, basically, homosexuality is caused by psychogenic, or non-hormonal, or psychological factors." Ibid.

homosexuality, Neustatter divides 'homosexuals' into two groups: bisexuals and "complete inverts." He postulates that:

> In the bisexuals [as opposed to exclusive homosexuals who, in his opinion, "are probably glandularly determined, although at present there is no proof of this"] psychological explanations are relevant, although even here one must assume some constitutional predisposition. The main explanation is offered by the psychoanalytic school.[230]

In spite of this, beginning in the early 1950s, many biologists[231] (and some psychologists[232]) came to discount Freudian and Freudian-inspired theories concerning the origin and characteristics of homosexuality. This is in part because biologists in general (and behavioral endocrinologists in particular) are more interested in discovering biological mechanisms behind behavior, and in part because it became apparent that

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[230] Although he concludes that "to my mind such explanations are too simple to account for such gross disturbances of function." Neustatter, W. L. (1954). "Homosexuality: The Medical Aspect." The Practitioner **172**(1): 364 - 373.

[231] See, for instance, Laidlaw, R. (1952). "A Clinical Approach to Homosexuality." Marriage and Family Living **14**(1): 39 - 46. Karin Martin speculates:

> This move toward attributing homosexuality to physiological factors may have been one to draw more rigid boundaries around the scientific expertise of the medical profession and to move away from "unscientific" psychoanalytic claims.

in Martin, K. (1993). "Gender and Sexuality: Medical Opinion on Homosexuality, 1900-1950." Gender and Society **7**(2): 246-260.

[232] There have always been psychologists skeptical about the possibility of "curing" homosexuality through psycholanalysis. Various review articles hace drawn attention to the difficulty of finding confirmation of successful "talking cures." E.g., Curran, D., and D. Parr (1957). "Homosexuality: An Analysis of 100 Male Cases Seen in Private Practice." British Medical Journal **1**: 767-801. See also Saghir, M. a. E. R. (1973). Male and Female Sexuality. Baltimore, Williams and Williams. And finally, Hemphill, R., et. al. (1958). "A Factual Study of Male Homosexuality." British Medical Journal **1**: 1317-1322.

Freudian and Freudian-inspired psychoanalytic attempts to "cure" homosexuality were demonstrable failures.[233] John Money, in his 1965 foreword, writes:

> In an earlier era, psychodynamic explanations captured enthusiasm and prompted research. But psychodynamics did not follow through with the promised payoff in terms of scientific prediction and control of sexual pathology.[234]

A decade later, Acosta, in his historical review of the etiology and treatment of homosexuality, concludes:

> It seems that neither behavioral therapy nor psychoanalytic therapy has convincingly proven to be effective in the treatment of either male or female homosexuals. What is clear is that both methods have had minimal successes and an overwhelming number of failures.[235]

Besides the inability to fulfill the goal of curing homosexuality, many researchers began to abandon Freudian and Freudian-inspired theories because they did not fulfill key

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[233] Laidlaw writes:

> Although in the past there have been complete cures of homosexuals claimed by psychoanalysts in various schools, I think that there is a trend, as time has gone on, among psychiatrists themselves to feel less confident that all cases are curable.

Laidlaw, R. (1952). "A Clinical Approach to Homosexuality." Marriage and Family Living **14**(1): 39 - 46.

[234] Money, J. (1965). Foreword. Sex Research: New Developments. J. Money. New York, Holt, Rinehart and Winston.

[235] Acosta, F. (1975). "Etiology and Treatment of Homosexuality: A Review." Archives of Sexual Behavior **4**(1): 9 - 29.

scientific criteria – both conceptual[236] and procedural. Conceptually, psychoanalytic theories could not account for developmental outcomes that deviated from etiological predictions (e.g., male homosexuals who grew up with "warm and affectionate"[237] relationships with their fathers.) In terms of procedure, it is not clear how psychoanalytic studies (and hence attempts at cures) can utilize control groups or double-blind testing. In his historical review of methods used to alter (homosexual) sexual orientation, Timothy Murphy writes:

> Virtually every [psychodynamic] study mentioned above failed to establish any control mechanism for the intervention being tested. It is thus impossible to tell whether the "successes" reported belong to the charm of the therapist or to the technique, were the result of psychosexual developmental changes occurring for reasons unrelated to the theory, were the consequence of the psychologically powerful placebo effect or lasted. One study that did utilize a scientific control found that a psychotheraputic program of reorientation had no demonstrable benefit.[238]

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[236] Gadpaille, summarizing his section giving a historical review of psychoanalytic theories of the etiology of homosexuality, concludes:

> The shortcomings in our present knowledge of homosexuality lie not necessarily in fallacies in that knowledge; all of the theoretical contributions have proven to explain some aspects and incidences of the disorder, and some of them may explain most. But there remain so many unexplained cases, so many of which seem, at least, not to be adequately elucidated by existing [psychodynamic] concepts. It is with the hope that newer biological research may illuminate a few of the obscure corners of its origin that this review is undertaken.

Gadpaille, W. (1972). "Research into the Physiology of Maleness and Femaleness: Its Contributions to the Etiology and Psychodynamics of Homosexuality." Archives of General Psychiatry **26**(3): 193-206.

[237] Ibid.

[238] Murphy, T. (1992). "Redirecting Sexual Orientation: Techniques and Justifications." The Journal of Sex Research **29**(4): pp. 501 - 523.

Because of the failures of psychoanalysis to determine the etiology and treatment of homosexuality, endocrinologists, in general, looked to hormones as the causal factor.

III.Endocrine Imbalance

However, the only promising biological model (that, unlike Beach's, treated homosexuality as a pathology), until the advent of the organization/activation model, was of persistent hormonal imbalances in adulthood. While it had long been speculated that homosexuals had "humoral" imbalances, the chemical isolation of androgens and estrogens led some scientists to postulate an imbalance between these specific hormones as the cause of homosexuality.[239] Specifically, male homosexuals[240] were thought to have

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[239] Beach argued consistently against this, pointing out that the results of numerous studies argue "against any interpretation of homosexuality as the direct consequence of endocrine pathology." Beach, F. A. (1953). "Animal Research and Psychiatric Theory." Psychosomatic Medicine **15**(5): 374 - 388.

[240] Researchers have focused almost exclusively upon male homosexuality. There are a number of reasons for this, both ideological and methodological. The most obvious (methodological) reason for the focus on males is the perceived complication of the menstrual cycle in women. In their study of androgen metabolism, Tourney and Hatfield write:

> Biological aspects of psychosexual disturbances in schizophrenia and homosexuality have been attempted by a number of investigators since the time of Kraepelin. Various endocrine disorders were thought to play a role in both these disorders, but none of the results have been definitive. Understandably, because of sex hormone differences between males and females, most investigations have been carried out in male subjects.

Tourney, G., and Lon M. Hatfield (1973). "Androgen Metabolism in Schizophrenics, Homosexuals, and Normal Controls." Biological Psychiatry **6**(1): 23 - 36.

lower levels of circulating androgens and higher levels of estrogens than found in heterosexual men, thus accounting for their "feminine" behavior.[241]

However, laboratory results did not support this hypothesis. Studies of rats and guinea pigs could not find any differences in plasma testosterone and estradiol concentrations in males that responded by lordosis to male mounts and those who did not.[242] Human studies either found no difference, or were contradictory: some found lower plasma testosterone concentrations in homosexual men, while others found elevated levels.[243]

But as chemical assays and testing techniques became more accurate, the hormonal levels of male homosexuals proved to be frustratingly normal. For instance, William Perloff, reporting on the results of his endocrine clinic, notes that:

> Homosexuality is still considered by many to be a manifestation of endocrine imbalance, and reports purport to prove that abnormal ratios of androgen to estrogen may be the basis for homosexuality . . . In our experience, no patient, either male or female, has shown any consistent reversal of the endocrine pattern

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[241] The author of one study, finding higher levels of estrogens in a group male homosexuals (but normal androgen levels), concluded:

> In the face of such highly suggestive hormonal differences one may assume that such data point to a definite biologic mechanism in homosexuality. Of course it is not possible at this time to evaluate the true significance of the difference, but it seems that the constitutional homosexual has a different sex hormone chemistry than the normal male.

Glass, S. J., et. al. (1940). "Sex Hormone Studies in Male Homosexuality." Endocrinology **26**(4): 590 - 594.

[242] Aron, C., et. al. (1991). Heterotypical Sexual Behaviour in Male Mammals: The Rat as an Experimental Model. Heterotypical Behaviour in Man and Animals. B. Haug, Aron. London, Chapman and Hall.

[243] Nieschlag, E. (1978). The Endocrine Function of the Human Testis in Regard to Sexuality. Symposium on Sex, Hormones and Behaviour, London, Excerpta Medica.

> to explain homosexual tendencies. We have never observed any correlation between the choice of sex object and the levels of hormonal excretion.[244]

The etiology of homosexuality was (and remains, in spite of the protestations of a few psychoneuroendocrinologists) a mystery. This mystery was, for those inclined towards "hormonal" explanations, a crucial one, as it appeared to involve the very activities mediated by gonadal hormones, yet could not be explained through laboratory findings. The tremendous explanatory promise of endocrinology appeared to be at an impasse when it came to the phenomenon of homosexuality.

In short, the presumed causal factor responsible for homosexuality was missing. When a presumed casual factor cannot be determined, one option is to propose another factor. Some scientists did this, postulating a genetic component to homosexuality (a field of research that continues to this day). However, because the field of genetics was still quite primitive at this time, the only venue for research was twin studies. While these studies did provide some evidence of a genetic link, it was hardly conclusive. Twin studies have the additional problem of only being able to control for one factor – genetic makeup – while being unable to account for experiential factors in particular and environmental factors in general. For this reason, many researchers continued to look to hormones for an explanation of homosexuality.

In addition to the ambiguities and uncertainties of genetics studies, there was also a train of thought from the history of endocrinology: behaviors whose manifestation were thought to be due primarily to genetic factors were considered instinctive (such as the "scratch reflex"). While certain sexual behaviors (such as mounting and lordosis) could

[244] Perloff, W. H. (1949). "Role of Hormones in Human Sexuality." Psychosomatic Medicine: Experimental and Clinical Studies **11**(3): 133 - 139.

be considered “instinctive” in the broad sense of the term, endocrinologists had many lines of evidence indicating that these “instinctive” behaviors are heavily mediated by hormones. As such, endocrinologists rejected the simple model of phenotypic outcome as the result of the combination of genotype and environment, and adopted a more complicated model of phenotypic development, one in which both genetic and environmental influences mediate and are mediated by hormones.

More specifically, genetic factors can determine hormone production and influence (as in the cases of Congenital Adrenal Hyperplasia, a genetically caused overproduction of androgens, and Complete Androgen Insensitivity Syndrome, wherein androgens are produced but cannot be recognized by the body) and environmental factors can influence the hormonal milieu (in terms of stress or early experience). Thus, in spite of the disappointing results of the homosexuality studies, endocrinologists in general were loath to abandon hormones as a causal factor in the etiology of homosexuality.

The organization/activation model provided a solution: hormonal abnormalities *in utero* were responsible for later abnormal behavior by preventing the normal masculine or feminine development of the fetal brain. While the abnormal hormonal influences vanished after birth, their original imprint remained, thus explaining both the deviant behavior of homosexuals and their normal, adult, hormone levels.

IV. Psycho-Neural Pseudo-Hermaphroditism

A major proponent of this model of the origin of homosexual behavior was Gunther Dörner, who explains heterosexual, bisexual and homosexual behavior as the result of "different degrees of androgen deficiency in males and androgen excess in females during sex-specific brain differentiation,"[245] As a result of atypical hormone levels during this critical period of development, the neural systems of these individuals develop in a "pseudo-hermaphroditic" fashion. More specifically:

> An androgen deficiency in genetic males during a critical period of brain organization gives rise to predominantly female differentiation of the brain. This androgen deficiency in early life can be largely compensated by increased hypophyseal gonadotropin secretion in later life. Thus, the predominantly female-differentiated brain is postpubertally activated by an approximately normal androgen level, leading to homosexual behavior.[246]

This model of the origins of homosexual behavior was appealing. It combined the earlier doctrine of endocrine imbalances with the organization/activation model in such a way as to explain the phenomena of normal adult steroid levels. In addition, and contrary to Beach's model, homosexuality was pathological, and not part of the spectrum of normal development. In their review of the role of prenatal hormones on psychosexual development, Anke Ehrhardt and Heino Meyer-Balhburg note that:

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[245] Dorner, G. (1978). Hormones and Sexual Differentiation of the Brain. Symposium on Sex, Hormones and Behaviour, London, Excerpta Medica.

[246] Ibid.

> [S]ince the discovery of sex steroids, the development of homosexuality – defined as a lasting sexual orientation towards the same sex . . . has been repeatedly ascribed to endocrine abnormalities. No wonder then, that the psychoendocrine hypothesis was reformulated in terms of prenatal hormone effects when animal research documented the important function of pre-and peri-natal androgens in the sexual differentiation of the brain and the subsequent development of sex-dimorphic behaviour.[247]

Instead of dismissing hormones as a causal factor, this conception of the etiology of homosexuality simply changed *the point in time* at which hormones were causally effective.

Dörner's hypothesis has had tremendous staying power. William Byne, in his critical historical review of psychobiological research on sexual orientation, writes:

> Some of the same hormones that participate in masculinization of the rodent brain also participate in masculinization of the external genitalia. Thus, one might question how the prenatal hormonal theory could account for exclusive homosexuality in individuals with normal genitalia for their genetic sex. The

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[247] Ehrhardt, A. A., and Meyer-Balburg, Heino (1978). Psychosexual Development: An Examination of the Role of Prenatal Hormones. Symposium on Sex, Hormones and Behavior, London, Excerpta Medica. In his extensive 1984 review of psychoendocrine research into the etiology of sexual orientation, Meyer-Bahlburg writes:

> During the past decade, the major focus of psychoendocrine theories of sexual orientation has shifted from the hormone situation in adulthood to the role of prenatal hormones . . . Currently, this theory enjoys widespread acceptance not only among biologists and physicians but also by behavioral scientists who are dissatisfied with the status of psychosocial explanations and by behavior therapists frustrated by the low success rate of their methods in changing sexual orientation.

Meyer-Bahlburg, H. (1984). "Psychoendocrine Research on Sexual Orientation: Current Status and Future Options." Progress in Brain Research **61**: 375 - 398.

concept of the "critical period" [for sexual differentiation of the brain] is often invoked to account for this discrepancy.[248]

However, this tidy explanation of (male[249]) homosexuality did not have a scrap of experimental evidence to support it. Much like Einstein's solution to the incompatibility of Newtonian relative motion and the constant speed of light, Dörner's solution to the "problem of homosexuality" explained the normal adult hormone levels of homosexuals while respecting the foundational assumption of its pathology. Dörner's hypothesis, though abstract in character, inspired a research program dedicated to finding the feminine in male homosexuals (a program in existence to this day).

On this model, the causal efficacy of androgens (or lack thereof) is split into two points of development. First, and most importantly, during the prenatal period, the neural tissues are permanently masculinized to various degrees depending upon the levels of circulating androgens. Second, hormones released during puberty "activate" the already-determined neural circuitry.

V. Empirical Confirmation through Behavioral Studies

Six years after Pheonix et. al. initially presented it, a team of psychologists, led by John Money, attempted to extend the organization/activation model to humans. He

[248] Byne, W. (1995). "Science and Belief: Psychobiological Research on Sexual Orientation." Journal of Homosexuality **28**(3/4): 303 - 344.

[249] While later researchers investigated Dörner's initial, vague hypothesis of the origin of female homosexuality (studying women and girls with Congenital Adrenal Hyperplasia), Dörner focused on finding the female in male homosexual brains, and program continued by Simon LeVay.

postulated that the same endocrine abnormalities that produced ambiguous genitalia would produce ambiguously gendered brains.[250]

Money and his team worked at the Johns Hopkins Medical School psychohormonal unit. The unit was set up with the express purpose of researching "the possible effects of exposure to excess fetal androgen on subsequent behavior and gender identity in certain clinical populations."[251] Specifically, they wanted to test the hypothesis that, just as prenatal androgen organized the sexual behavior of lab animals, it also organized the sexual (and gendered) behavior of humans.

But how to distinguish internal from external factors, that is, the effects of hormones from environmental influences? Money and his collegues thought they could make this distinction by studying "Nature's mistakes" – individuals with endocrinological or genetic defects that prevented normal hormonal development.[252] (A program of research that lasted until the mid-1990s.) Because it was known in advance that these individuals had "mixed" causative factors (hormones), it was believed that these non-exemplary examples of the organizational hormonal milieu would produce

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[250] After reviewing Jost's experiments, Money comments that

> Mammalian masculine anatomy, as these experiments show, is brought about by something added, failing which the more basic disposition of the embryo asserts itself. One wonders whether to look for a parallel in human psycho-sexual differentiation.

Money, J. (1965). Foreword. Sex Research: New Developments. J. Money. New York, Holt, Rinehart and Winston.

[251] Ehrhardt, A. A., et. al. (1968). "Fetal Androgens and Female Gender Identity in the Early-Treated Adrenogenital Syndrome." The Johns Hopkins Medical Journal **122**(3): 160 - 167. Note that the focus of the research is androgens in particular, rather than gonadal hormones in general. This is in part the result of Money's adoption of the "default" model.

[252] The language of "normal" versus "pathological" development pervades the literature of this time.

neural structures intermediate between the paradigmatic male or female brain, which would in turn produce "mixed" behavior that could be studied. Money explicitly adopted the organization/activation model for his investigations of "pseudohermaphrodites" – individuals with ambiguous genitalia as the result of abnormal hormone exposure.

Money became interested in the psychosexual development and behavior of pseudohermaphrodites as a part of his long-term work, which was:

> [E]nhanced by findings stemming from animal studies. Phoenix, Goy, Gerall and Young . . . ventured the hypothesis that prenatal androgen had affected neurosexual organization [of the guinea pigs], and thus, the organization of behavior.[253]

As will be discussed in the final chapter, Money considered human psychosexual behavior to be a broad category, including sexual orientation, gender identity, aggression, physical activity, and career goals.

While the organization/activation model was assumed by many to apply to humans, the fact that the masculinized guinea pigs used in the original experiment were a laboratory creation (as well as the challenges inherent in finding an animal correlate to gender identity) created difficulties in extending the model to humans. In order to determine if this extension was justified, researchers needed to find a human correlate to the hormonally manipulated laboratory animals. Money came up with a solution to this difficulty:

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[253] Ehrhardt, A. A., and Money, John (1967). "Progestin-Induced Hermaphroditism: IQ and Psychosexual Identity in a Study of Ten Girls." The Journal of Sex Research **3**(1): 83 - 100.

> There is a somewhat suggestive human parallel to the animal experiments with androgen to be found in human female hermaphrodites with the adrenalgenital syndrome, virilized in utero from an excess of adrenal androgens.[254]

What Money here calls the "adrenogenital syndrome" later became known as "congenital adrenal hyperplasia," or CAH, a condition that causes excess production of androgens *in utero*. It was hoped that these females could be human models for the masculinization of the brain by androgens, and thus serve as a crucial test for the extension of the organization/activation hypothesis to humans. Not only could scientists determine the effects of abnormal hormonal exposure on sexual orientation, they could also determine their effects on gender identity.[255] In this way, Money and his collegues hoped to tease apart the relative influences of internal and external factors on psychosexual development.

Two of Money's students who published the most influential articles continuing his general project are Anke Ehrhardt and Heino Meyer-Balhburg. One of their early

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[254] Money, J. (1965). Foreword. Sex Research: New Developments. J. Money. New York, Holt, Rinehart and Winston.

[255] In general, the scientific community accepted this uncritical extension of the model to humans at this time (and for the next twenty to thirty years). For instance, in their 1981 review, Rubin et. al. note:

> Many investigators are attempting to extend the data regarding the postnatal gonadal steroid activation of sexually dimorphic behaviors from animals to man. Relevant information is being obtained by the observation of behavior and concomitant evaluation of hormone levels in subjects whose hormonal status or behavioral repertoire furnishes an opportunity to study conditions other than normal ones. [Reflecting Lillie's methodological emphasis on the atypical.] These include individuals who exhibit unusually high or aberrant levels of sexually dimorphic behavior or who suffer from clinical endocrine syndromes that mimic certain experimental animal manipulations.

Rubin, R., et. al. (1981). "Postnatal Gonadal Steroid Effects on Human Behavior." Science **211**(4488): 1318 - 1324.

(1968) studies found that, in comparison to controls, girls with the adrenogenital syndrome (CAH) displayed significantly higher incidences of tomboyism, which they rather vaguely defined as possessing a high energy level and a minimum interest in doll play, dresses and girls' activities.[256]

While Ehrhardt et. al. mention that increased tomboyism could be associated with higher socioeconomic class, they take more seriously the possibility that tomboyism could be related to high IQ. In support of this possibility, they point to studies by Sontag and collegues at the Fels Institute at Temple University School of Medicine indicating that children or either sex with high IQs:

> [W]ere competitive, self-assertive, independent and dominant in interaction with other children – not very feminine characteristics according to traditional stereotype. One of the Fels workers summarized the issue by saying that the simplest way to describe the developmental history necessary to make a girl into an intellectual person is that "she must have been a tomboy at some point in her childhood."[257]

Because of this purported connection between high IQ and tomboyism, Ehrhardt et. al. conclude that:

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[256] Ehrhardt et. al. note that:

> While there was no girl in the group who was labeled a tomboy for most of her life, eleven of the patients [out of a total of fifteen] were described as tomboys by themselves and their mothers throughout childhood.

Ehrhardt, A. A., et. al. (1968). "Fetal Androgens and Female Gender Identity in the Early-Treated Adrenogenital Syndrome." The Johns Hopkins Medical Journal **122**(3): 160 - 167.

[257] Ibid.

> It would appear therefore that tomboyism in girls with the adrenogenital syndrome has something to do with the syndrome itself. The responsible factor could be a genetic one, since the syndrome is known to be genetically recessive in etiology. Or, it could be a fetal adreno-cortical effect . . . in each case on the hypothalamus or a related area of the brain.[258]

It becomes clear that Ehrhardt et. al were inclined to believe the second scenario: that the relevant causal factor in tomboyish behavior was hormonal, not genetic. This reflects the explanatory promise of hormones. They summarize their conclusions as follows: "The findings of this present study suggest that certain aspects of gender dimorphic behavior can be modified by fetal androgens in the human female."[259] (Later studies retracted this claim, noting that girls coming in for treatment tended to come from financially well-off families, whose parents themselves had above-average IQs.)

In 1981, Anke Ehrhardt and Heino Meyer-Balhburg published "Effects of Prenatal Sex Hormones on Gender-Related Behavior" in *Science*, summarizing almost a decade of research, which was to become the most influential article inspired by Money's project. While Money and his students had published their findings before, it was the special issue of *Science* dedicated to the application of the organization/activation model to human beings, focusing on the work of Ehrhardt and Meyer-Balhburg, that caused a revolution in endocrinological and psychological thought.

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[258] Ibid.

[259] Ibid.

To test further the hypothesis that prenatal androgen exposure could masculinize behavior (including sexual orientation), Ehrhardt and Meyer-Balhburg studied the behavioral and tempermental tendencies of girls with CAH. They examined four areas of behavior within this context: gender identity, defined as an individual's identity as belonging to one of the two sexes; gender role behavior, "including all those aspects of behavior in which normal boys and girls differ from one another in our culture and at this particular time in history;" sexual orientation; and general intelligence and cognitive sex differences.[260]

In particular, the scientists were interested in noting the tendencies of CAH girls to exhibit "masculine" behavior, in part because this is the most plausible extension of animal experiments to human behavior. While correlating animal models to human cognition, sexual orientation and, especially, gender identity is fraught with conceptual problems, Ehrhardt and Meyer-Balhburg (and others) could easily apply animal behavioral studies of energy expenditure, social aggression, parenting rehearsal, patterns of group interaction and grooming behavior to human gender role behavior. For human children, "masculine" or "tomboy" behavior is operationally characterized as preference for outdoor activities, preference for male over female playmates, greater interest in a career than housewifery, and less interest in "play rehearsal of motherhood roles."[261]

To determine the level of masculine or tomeboy behavior, Ehrhardt and Meyer-Balhburg questioned the girls' parents as well as their teachers about their activity levels, play and clothing preferences, and career ambitions. In addition, older CAH girls were

[260] Ehrhardt, A., and Meyer-Bahlburg, Heino (1981). "Effects of Prenatal Sex Hormones on Gender-Related Behavior." Science **211**(20): 1312 - 1318.

[261] Ibid.

questioned about their sexual fantasies. They used three different designs for their studies: comparing CAH girls with age-matched normal controls; with their unaffected siblings; and with a clinical contrast group.

In reviewing their studies, Ehrhardt and Meyer-Balhburg found that, while prenatal androgenization does not appear to affect gender identity formation directly, it seems to influence gender role behavior:

> [T]he behavior of the prenatally androgenized girls differed significantly from that of the controls in that they typically demonstated (i) a combination of intensive active outdoor play, increased association with male peers, long-term identification as a "tomboy" by self and others, probably all related to high energy expenditure, and (ii) decreased parenting rehearsal such as doll play and baby care, and a low interest in the role rehearsal of wife and mother versus having a career.[262]

In terms of social aggression, the results were less conclusive. While CAH girls were more likely to participate in "rough and tumble play," they were no more likely to initiate fights than their unaffected siblings or controls.

The findings on sexual orientation proved to be more contentious. Ehrhardt and Meyer-Balhburg note that:

> With the recent advances in psychoneuroendocrine research, prenatal hormones have also been implicated [in having a causal role in the formation of sexual orientation]. If early androgenization or deandrogenation can determine male and

[262] Ibid.

> female patterns of mating behavior in lower mammals, it is tempting to extrapolate from these findings to the human situation as suggested by Dörner.[263]

Ehrhardt and Meyer-Balhburg refer to the theory proposed by Dörner as the "prenatal hormone theory." Because of their *in utero* androgenization, those CAH girls who have reached puberty provide an ideal test case of Dörner's theory.

The prenatal hormone theory:

> [P]redicts that the effective presence of androgen in prenatal life contributes to the development of sexual orientation towards females, and that a deficiency of prenatal androgens or tissue insensitivity to androgens leads to a sexual orientation towards males, regardless of the genetic sex of the individual.[264]

Accordingly, the prenatal hormone theory would predict that CAH girls, upon reaching puberty, would have a predisposition towards lesbianism. In their earlier 1968 article, Ehrhardt and Meyer-Balhburg did not find high levels of homosexuality. Focusing upon CAH women whose underwent early treatment, Ehrhardt et. al. found that the majority of CAH women interviewed were heterosexual, some were bisexual, and none were homosexual.[265] A similar study in the Soviet Union found that approximately

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[263] Ibid.

[264] Ibid.

[265] Ehrhardt et. al. conclude that:

> Their tomboyism did not include implications of homosexuality or future lesbianism, or a belief of having been assigned to the wrong sex.

Ehrhardt, A. A., et. al. (1968). "Fetal Androgens and Female Gender Identity in the Early-Treated Adrenogenital Syndrome." The Johns Hopkins Medical Journal **122**(3): 160 - 167.

half the subjects were heterosexual, half bisexual, and none homosexual. From these results, Ehrhardt and Meyer-Balhburg conclude that "a rigidly deterministic effect of prenatal androgens on sexual orientation appears to have been ruled out."[266]

Later studies, however, provide more evidence is support of the prenatal theory. That is to say, as the initial clinical population of CAH girls grew into maturity, Ehrhardt and Meyer-Balhburg had a larger group to study. These follow-up studies found that, not only did CAH girls display more "tomboy" behavior, they also had a higher tendency towards lesbianism. Meyer-Balhburg, in his 1984 review of endocrinological research on sexual behavior, notes that:

> In a recent controlled follow-up study of the Hopkins sample of early-treated CAH women in comparison to women with androgen insensitivity or Müllerian duct aplasia, the CAH women had a significantly increased bisexuality in imagery and/or sexual experience although here also the majority were heterosexual. Although these results are compatible with the prenatal hormone theory, they are also open for a social-learning interpretation if one assumes that the awareness of the medical condition on the part of the parents or the patients may have influenced their psychosexual development. Not enough data are available to clarify this point.[267]

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[266] Ehrhardt, A., and Meyer-Bahlburg, Heino (1981). "Effects of Prenatal Sex Hormones on Gender-Related Behavior." Science **211**(20): 1312 - 1318.

[267] Meyer-Bahlburg, H. (1984). "Psychoendocrine Research on Sexual Orientation: Current Status and Future Options." Progress in Brain Research **61**: 375 - 398.

The prenatal hormone theory, as initially espoused by Dörner, was not directly supported by the evidence. More data soon became available. Follow-up studies by Money (1988) and Meyer-Balhburg (1993) lead the latter to conclude:

> The data suggest that, in either genetic male or female individuals (i.e., independent of chromosomal sex), some degree of prenatal exposure exposure to and utilization of androgens seems to "facilitate," but not to fully determine the development of erotic atrraction to female individuals as postulated by the prenatal hormone theory.[268]

Combining these results with earlier findings on gender *identity*, Meyer-Balhburg, Ehrhardt, and their colleagues conclude that, while gender identity did not appear to be affected by prenatal androgen exposure, gender role and sexual orientation did. Subsequently, many scientists researching the etiology of sexual orientation have accepted these conclusions, and use them as a basis for further research. This will be discussed more thoroughly in subsequent chapters.

These series of studies on CAH girls (especially the 1981 study that appeared in *Science*) were tremendously influential. Among other things, many endocrinologists interpreted them to "all show that both gender-related behavior and genital morphology are subsequently affected by levels of steroid hormones present during prenatal development."[269]

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[268] Meyer-Bahlburg, H., et. al. (1995). "Prenatal Estrogens and the Development of Homosexual Orientation." Developmental Psychology **31**(1): 12 - 21.
[269] MacCulloch, M., and Waddington, John (1981). "Neuroendocrine Mechanisms and the Aetiology of Male and Female Homosexuality." The British Journal of Psychiatry **139**(4): 341 - 345.

The vast majority of endocrinologists (judging by the articles citing Ehrhardt and Meyer-Balhburg's work) uncritically accepted their conclusions. Bruce McEwen, in an article appearing in the same issue of *Science* as Ehrhardt and Meyer-Balhburg's influential report, describes this study as being able to:

> [E]laborate on the extent to which we are able to recognize, in spite of the environmental influences of learning, the components of human behavior which are influenced by hormones during development and in adulthood.[270]

That is, the work of Ehrhardt and Meyer-Balhburg could provide a means of distinguishing hormonal from environmental influences on human behavior.

In the same issue, Rubin and his colleagues, reviewing studies of postnatal effects of hormones on human behavior, refer to the work of the Johns Hopkins Psychohormone Unit to note that:

> Prenatal exposure of humans to gonadal steroids, whether of internal or external origin, appears to have an appreciable influence on behavioral development. In particular, exposure of the female to androgens or androgen-based progestins increases the frequency of tomboyish behavior during childhood.[271]

In other words, the results of CAH studies appear to confirm the organization/activation model for human beings. More specifically, they appear to confirm Dörner's prenatal hormone theory – that sexual orientation, although not

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[270] McEwen, B. S. (1981). "Neural Gonadal Steroid Actions." Science **211**(4488): 1303 - 1311.

[271] Rubin, R., et. al. Ibid."Postnatal Gonadal Steroid Effects on Human Behavior." 1318 - 1324.

necessarily gender identity, is dependent upon the organizing effects of prenatal androgens. However, we should note that this confirms that *female* homosexuality depends upon prenatal organization, not male.

One scientist who did not accept this conclusion was Froukje Slijper, a child psychiatrist working in the Netherlands. In his critical 1984 review, he begins by noting that:

> The explanation for tomboy behaviour [of CAH girls] is sought by Ehrhardt et. al. in the prenatal action of the male hormone. According to these authors, the male hormone has an "imprinting effect on the central nervous system," which gives rise to tomboy behaviour.[272]

Slijper is hesitant to adopt this explanation, for two reasons. First, the tomboy behavior displayed by CAH girls could be attributed to the way in which the parents react to the child's masculized genitalia. Many experiments demonstrate that parents (and adults in general) react differently to male and female infants. For instance, parents often exhibit significantly different behavior towards a baby in male clothing and a male name than towards that same baby when dressed as a girl and given a female name.[273] From this, Slijper concludes that the masculinized genitalia of CAH girls can create doubts in the minds of the parents about the child's sex.[274]

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[272] Slijper, F. (1984). "Androgens and Gender Role Behaviour in Girls with Congenital Adrenal Hyperplasia (CAH)." Progress in Brain Research **61**: 417 - 422.

[273] Will, J., et. al. (1976). "Maternal Behavior and Perceived Sex of Infants." American Journal of Orthopsychiatry **46**: 135 - 140.

[274] Slijper, F. (1984). "Androgens and Gender Role Behaviour in Girls with Congenital Adrenal Hyperplasia (CAH)." Progress in Brain Research **61**: 417 - 422.

Second, CAH is a chronic, and often serious, illness. CAH girls are often hospitalized, as many of them often undergo at least two genital operations, one immediately after birth and another in adulthood. Girls with the more serious version of CAH (the salt-loss variety) are frequently and often seriously ill in their first years of life. In addition, all CAH females have to take hydrocortisone for the rest of their lives.[275]

Slijper notes that chronically ill children often compensate for feelings of insufficiency and insecurity with confident and "bustling" behavior.[276] In addition, and not surprisingly, chronically ill children are often anxious about the future, an anxiety that can manifest itself as a lack of interest in marriage, motherhood, and responsibility for small children.[277] Because of these behavioral tendencies of chronically ill children, Slijper suspects that the potential severity of CAH could act as a confounding factor in the results of Ehrhardt and Meyer-Balhburg. This, plus parental ambiguity about their child's gender identity, could explain the high levels of tomboyism found in CAH girls.

To test this possibility, Slijper compared the behavior of CAH girls with that of other chronically ill girls (suffering from diabetes mellitus), the healthy sisters of CAH girls, and controls. Similarly, Slijper compared the behavior of boys with CAH, their unaffected brothers, diabetic boys, and a control group.

To measure, and hence compare, the gender role behavior of these children, Slijper used the Sophia test, which is based upon those aspects of gender role behavior as

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[275] Ibid.

[276] E.g., Tavormina, J., et. al. (1976). "Chronically Deviant Population?" Journal of Abnormal Child Psychology **4**: 99-111.

[277] Schowwalter, J. (1979). The Chronically Ill Child. Basic Handbook of Child Psychiatry. J. Noshpitz. New York, Basic Books. **1:** 432-436.

distinguished by Ehrhardt et. al. Values the children attached to indoor and outdoor play, playing with girls as opposed to boys, dolls versus cars, as well as marriage and parenthood were measured and scored, with higher scores indicating more "girlishness." Slijper initially gave this test to the control group with the purpose of establishing a scale on which boys were to be distinguished from girls.[278]

When administering the Sophia test to the sick children, Slijper also interviewed their parents, "using precoded questions about the children's psychosexual and psychosocial development,"[279] in addition to collecting medical data on the degree of virilization before genital operations. The purpose of these additional measures was to compare parental perception with the Sophia scores, as well as to determine what, if any, effect the degree of virilization has on both.

The chronically ill girls (both CAH and diabetes) had significantly more "boyish" scores on the Sophia test than did the controls. From this, Slijper concludes that "the effect on gender role behavior is not necessarily explained by hormonal action alone; *being sick plays a role*."[280] [Original emphasis] Examining the data on ill girls more carefully, Slijper found that CAH girls scored significantly more "boyishly" than did diabetic girls. However:

> Closer examination of the data revealed that the *specific CAH effect is fully accounted for by the group of girls with the salt-loss variant of CAH*; with CAH

[278] Slijper, F. (1984). "Androgens and Gender Role Behaviour in Girls with Congenital Adrenal Hyperplasia (CAH)." Progress in Brain Research **61**: 417 - 422.

[279] Ibid.

[280] Ibid.

> girls with the non-salt-loss variety about the same as diabetic girls. [Original emphasis][281]

This reinforces Slijper's claim that chronic illness can have a direct effect on a child's gendered behavior. More tellingly, the objective degree of virilization at birth did not correlate with the gender score, nor was it the case that CAH girls differed from control girls in their appreciation of "fighting, romping, wild play and outdoor play. However, more parents of a CAH daughter (80%) than of a diabetic daughter (50%) consider that their child is extremely fond of romping."[282] Although Slijper does not state so explicitly, the implication is that virilization can influence parents' perceptions of their child's behavior, even years after the beginning of treatment.

These findings lead Slijper to conclude that:

> [T]he hypothesis that behaviour is masculinized by exposure to androgen hormones during the early stages of development cannot be supported by this study. Psychosocial factors such as the child's being sick, and the parents' doubts about the sex of the child seem to have more influence on gender role behaviour than does androgenic hormone action (i.e. degree of virilization).[283]

In other words, the exclusive focus of previous CAH studies upon hormonal factors – a methodological influence of the organization/activation model – resulted in other, potentially salient, factors being ignored.

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[281] Ibid.

[282] Ibid.

[283] Ibid.

VI. Reaction of the Scientific Community

But it appears that Slijper's objections fell on deaf ears, as the vast majority of articles citing Ehrhardt and Meyer-Bahlburg's work appear to accept it uncritically. The authors of a few studies accept their results as supporting Dörner's prenatal hormone theory and, by extension, the organization/activation model, yet caution readers that the studies are hampered by methodological problems. Specifically, the results "are not fully consistent but may be construed to support"[284] the results found in lower animals. Other authors point out that the studies were afflicted with "research problems"[285] or "design weaknesses."[286] None of these authors elaborate on the nature of the methodological or design problems.

However, the majority of later articles do not mention any sort of methodological difficulties. Instead, the authors of these papers either reference the work of Ehrhardt and Meyer-Balhburg uncritically, as part of the general background information of the

[284] Mazur, A., and Booth, Alan (1998). "Testosterone and Dominance in Men." Behavioral and Brain Sciences **21**(3): 353 - 397.

[285] Marini, M. M. (1990). "Sex and Gender: What do We Know?" Sociological Forum **5**(1): 95 - 120.

[286] In contrast to Mazur and Booth, Wilson comments that "despite inherent weaknesses in design . . . the consistency of the findings in such studies is impressive." Wilson, J. D. (1999). "The Role of Androgens in Male Gender Role Behavior." Endocrine Reviews **20**(5).

field,[287] or use the results of their studies as the foundation for further research into the etiology of sexual orientation.

As a result of the crucial resolution of homosexuality, many, if not most, members of the scientific community accepted the notion that androgen alone is the causative factor in prenatal organization. This happened in spite of several prominent researchers trying to discourage single-factor models of development, including Charles Phoenix, one of the authors of the seminal 1959 paper. Speaking at a conference sponsored by the International Institute for the Study of Human Reproduction, Phoenix:

> [H]oped that the concept of the organizing action of prenatal androgen will not give rise to time-worn arguments of heredity versus environment or be conceived of as a fatalistic theory that renders useless the need for studying the effects of the environment on the development of normal sexual behavior.[288]

But give rise it did. The question of the influence of prenatal hormones on later sexual and gendered behavior was, almost from the beginning, debated in terms of nature (conceived of as internal factors) versus nuture (external factors).

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[287] E.g., Lalumiere, M., et. al. (2000). "Sexual Orientation and Handedness in Men and Women: A Meta-Analysis." Psychological Bulletin **126**(4): 575 - 595. Cleveland, H. H., Udry, J. Richard, Chantala, Kim (2001). "Environmental and Genetic Influences on Sex-Typed Behaviors and Attitudes of Male and Female Adolescents." Personality and Social Psychology Bulletin **27**(12): 1587 - 1598. Negri-Cesi, P., et. al. (2001). "Aromatase Expression and Activity in Male and Female Cultured Rat Hypothalmic Neurons: Effect of Androgens." Molecular and Cellular Endocrinology **178**(1): 1 - 10. Breedlove, S. M., and Hampson, Elizabeth (2002). Sexual Differentiation of the Brain and Behavior. Behavioral Endocrinology. B. Becker, Crews and McCarthy. Cambridge, MIT Press. Csatho, A., et, al. (2003). "Sex Role Identity Related to the Ratio of Second to Fourth Digit Length in Women." Biological Psychiatry **62**(2): 147 - 156.

[288] Phoenix, C. (1978). Prenatal Testosterone in the Non-Human Primate and its Consequences for Behavior. Sex Differences in Behavior. R. F. a. R. v. d. Wiele. Huntington, Robert E. Krieger Publishing Company.

For instance, psychologist Diane McGuinness, who studies gender differences in behavior, claims that many other psychologists disapprove of her research:

> Because the conclusion of all this seem to me inescapable, and it rides against the whole direction most of science has taken over the past twenty or thirty years [that most behavior is the result of socialization]. These things [cognitive differences between men and women] are not culturally induced. They're biological. Just as the capacity for language is prewired into our brains before birth – as Noam Chomsky, among others, has shown – so, in females, is a special skill in it. So is the male's special visual and spatial skill. And so, perhaps, are all the other abilities and behaviors I've talked about. What comes easy to either sex is likely to be biologically programmed, like the hypothalamus: stamped, primed, waiting to be developed.[289]

This echoes the metaphor of the developing brain as a photographic plate. As the reader may notice, her comments can be interpreted as having political, not just scientific, import.

Years later, Money decried the tendency of biologists and psychologists to follow a reductionist program in the explanation of sexual behavior. Theoretically, "they reduce the origins and development of human sexuality to a single and usually abstrusely defined determinant which typically belongs to one side or the other of the obsolete nature/nurture fence."[290] Money explicitly links the nature/nurture debate to politics, claiming that reductionists of either stripe:

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[289] From an interview with the authors, in Durden-Smith, J., and deSimone, Diane (1983). Sex and the Brain. New York, Arbor House. Original emphasis.

[290] Money, J. (1991). The Development of Sexuality and Eroticism in Human Kind. Heterotypical Behaviour in Man and Animals. B. a. A. Haug. London, Chapman and Hall.

> Wrongly equate the biological with the fixed and preordained, and the sociocultural with the unfixed and optional. By implication, the preordained is unmodifiable, and the arbitrary modifiable. Herein lurks another implication, a covertly political one. Scientists of the status quo favour a reductionist dogma of the biological unmodifiability of anything in men's and women's sexuality. Scientists of change favour another reductionist dogma, that of the sociocultural and environmental modifiability of everything in men's and women's sexuality.[291]

Perhaps Money is being uncharitable here; it is not clear that researchers in this area are reductionists in this manner. Nonetheless, Money's concern about the focus upon a single and "abstrusely defined" determining factor is a telling indictment of the rigidity of categories of sexual behavior and development that came with the adoption of the organization/activation model.

VII. Conclusion

Once homosexuality came to be seen as a distinct (and largely unitary) phenomenon, two elaborated hypotheses concerning the pathological nature of its etiology were available: that it was due to environmental factors; and that it was due to endocrine imbalance. As we have seen, neither elaborated hypothesis could explain adequately the phenomenon.

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[291] Ibid.

The organization/activation model was accepted, in part, because it provided a crucial resolution to the problem of homosexuality. The notion of central nervous system pseudohermaphroditism, while "solving" the problem of homosexuality, solved it in advance of any convincing empirical evidence. In providing this crucial resolution, it served as the deciding factor between two general theories of sexual development. Even though this resolution has the character of a thought experiment, it has shaped the development of the entire field.

The empirical confirmation of Dörner's prenatal hormone theory through CAH studies cemented its general acceptance within the scientific community, in spite of methodological problems. This largely uncritical acceptance reflects the power of crucial resolutions in general, and the crucial resolution of homosexuality in particular.

The organization/activation model also had the advantage of being able to explain both typical and atypical development. This tremendous explanatory promise can viewed as an exemplar both of unification and mechanism.

Chapter 6

Organization/Activation and Explanation by Unification

I. Introduction

The organization/activation model explains the etiology of a host of phenomena through one basic argument pattern: chromosomal arangement (and certain types of

external factors, if present) determine fetal hormone exposure; this hormone exposure determines, at least in part, both physiological and neurological development; the resulting neural structures determine later behavior and cognitive abilities.

Because one basic argument pattern explains both physical and behavioral developmental outcomes – previously thought to be unrelated – the organization/activation model appears to be an exemplar of what Philip Kitcher calls "explanation by unification." I claim that it *is* such an exemplar. However, because many endocrinologists explicitly describe their work in terms of mechanisms and the search for mechanisms, it is possible to apply the philosophical conception of mechanistic explanation to this field. (This is the topic of the next chapter.) I claim that viewing the model through a Kitcherian lens reveals both the strengths and the limitations of the unification approach to scientific explanation. Specifically, while Kitcher's ideal of explanatory unification, as applied to behavioral endocrinology, reveals several weaknesses in that account, there is still an important element of unification to the organization/activation model; a unification of mechanism *types*, not argument patterns.

To show this, I begin with a bit of intellectual history, outlining Kitcher's expansion and development of the unificationist account as initially put forth by Michael Friedman. Friedman considers and rejects several models of philosophical explanation, proffering the unificationist account in their stead. Next, to demonstrate the critical role explanatory unification played (and plays) in the development of the field of behavioral endocrinology, I show how well the organization/activation model satisfies Kitcher's ideal. However, there are limitations this appeal to unity has in terms of generating satisfactory explanations. Specifically, the same general argument pattern is used to

explain both homosexuality and transsexuality. I explore this problem in the ninth chapter. Finally, I address criticisms of Kitcher's account.

II. Intellectual Background

Advocates of the ideal of explanation by unification argue that we increase our scientific understanding of the world by creating and expanding upon a unified picture of it. The unification model of scientific understanding and explanation was first proposed by Michael Friedman in 1974 and elaborated upon by Philip Kitcher in the following decade. Friedman's initial paper was concerned with the connection between explanation and understanding – a connection he thought to be missing from theories of scientific explanation available at the time.

Intuitively, explanation confers the epistemic virtue of understanding. We seek explanations in order to understand the world around us. Friedman discusses and dismisses the Standard Model[292] and its associated deductive-nomological account, the "familiarity" account, and what he calls the "intellectual fashion" view as all inadequate to connect explanation to understanding. As other philosophers, criticizing the Standard Model, have pointed out, rational expectability does not confer understanding.[293] Because the inadequacies of the Standard Model and its associated deductive-

[292] As initially put forth by Hempel and Oppenheim in 1948. Hempel, C. (1965). Studies in the Logic of Explanation. Aspects of Scientific Explanation and Other Essays in the Philosophy of Science. C. G. Hempel. New York, The Free Press**:** 245 - 290.

[293] See, for instance, Scriven, 1959 and Salmon, 1971.

nomological account of scientific explanation are well known, I focus on Friedman's criticisms of the remaining two accounts.

One prominent account of understanding (inspired by the Logical Positivists' program of theory reduction) was that we explain unfamiliar events and phenomena (and thus understand them) by explicating them in terms of what we find familiar. This model of explanation, which relies heavily on analogy, is advocated by a wide variety of scientists and philosophers, from William Dray to Rom Harre´. Unfortunately, it is plagued with difficulties, the most prominent of which, according to Friedman, is it's failure to connect explanation to understanding.

Friedman denies that explanations produce understanding by reducing unfamiliar phenomena to familiar ones. On this general account of scientific explanation, science allows us to understand the world by relating and/or reducing unfamiliar phenomena to familiar ones. Thus, advocates of the familiarity account claim that the description of events or entities as analogous to familiar ones is a form of explanation. That unfamiliar entities can be explained implies (for advocates of the familiarity account) that these entities can be *understood*.

Analogy is the cornerstone of the familiarity account of explanation: it gives us a place to start our investigations, and suggests directions of research. The relationship between unfamiliar and familiar entities is one in which we can make inferences about the unfamiliar entities based upon what we know of the familiar ones. That which is explained (for example, sound) is explained by use of analogy to something with which we are familiar (for example, waves). We *understand* sound as something analogous to wave.

But we still need to discern exactly how analogical descriptions can provide explanations. One version of the familiarity account is that of simple reduction:

> I believe that examination will show that the essence of explanation consists in reducing a situation to elements with which we are so familiar that we accept them as a matter of course, so our curiousity rests.[294]

Although explanation, upon this account, involves descriptions, not all descriptions are explanations. I can describe the ice cube in my glass getting smaller the longer it is out of the freezer, but this does not explain why the ice cube gets smaller. The description does not give us an understanding of the phenomena of shrinking ice cubes. So one of the desiderata of the familiarity account is to distinguish explanatorily salient descriptions or comparisons from non-explanatory ones.

Friedman claims that the familiarity account is unable to fulfill this requirement for two reasons:

> 1. Many scientific theories relate familiar phenomena to unfamiliar ones (e.g. explaining water turning to steam when heated in terms of molecular bonds).
> 2. Being familiar does not equal being understood.[295]

The first objection is an empirical counter-example wherein the explanatory relation moves in the opposite direction: from the familiar to the unfamiliar. The second

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[294] P. W. Bridgeman, *The Logic of Modern Physics*, New York, Macmillian, 1968, p. 37, quoted in Friedman, M. (1974). "Explanation and Scientific Understanding." The Journal of Philosophy **71**(1).

[295] Ibid.

objection concerns the issue of distinguishing between explanatory and non-explanatory descriptions. I discuss these objections in order.

We are familiar with water turning to steam when heated; but the fact that we explain this phenomenon using unfamiliar entities such as molecular bonds and kinetic energy contradicts the familiarity account (according to Friedman). This counter-example is forceful, but its force can be mitigated by further reduction. Although we may be "unfamiliar" with molecules in terms of hands-on experience, we are quite familiar with the model of explanation supporting the theory of molecular bonds. A specific model, in this case, the billiard ball model of molecules, often is better understood than the system itself.[296] We can make predictions about the physical systems using the rules of the specific model, then refine the model by taking account of previously neglected features. For example, George G. Stokes developed the elastic sphere model of gas molecules from the billiard ball model by recognizing that the actual bodies were not rigid, and added equations of elasticity to the rules of the original model.[297] If we conceive of molecules as analogous to particles with forces of attraction (e.g., elastic bands), the model of explanation supporting molecular theory appears mundane. So, it is plausible that all explanatory appeals to unfamiliars will turn out to rely (at another level) on analogical extensions of the familiar.

It is the theoretical objection – that familiarity does not constitute understanding – that poses the strongest challenge to the familiarity account of explanation. Friedman claims that the familiarity account does not differentiate between descriptions that are

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[296] This example due to Hesse, M. (1953/4). "Models in Physics." The British Journal for the Philosophy of Science **4**.

[297] Ibid. See: Stokes, *Mathematical and Physical Papers I*, Cambridge, 1875, p. 75.

explanatory and those that are not. He points out that we are all familiar with household appliances, but most of us would be hard put to explain why they behave the way they do.[298]

At first, it appears that an advocate of the familiarity account can answer this objection by relying upon the maxim that, while all explanations are descriptions, not all descriptions are explanations. Thus, while I can open up and describe the various bits and pieces of the DVD player, for example, this description does not tell us why it behaves the way it does. This response, however, does not really answer Friedman's objection; it merely restates it. For, "being familiar, just like being expected, is not at all the same thing as being understood."[299] Another possible response (not addressed by Friedman) is to claim that we can explain unfamiliar phenomena by reducing them to phenomena we already understand – phenomena with which we are familiar. While this response provides a means to distinguish explanatory from non-explanatory descriptions, it does so at the cost of shedding any light on the elusive notion of understanding.

Friedman also considers and rejects the Standard Model (as initially promulgated by Hempel and Oppenheim), as well as the *Weltanshauung* (or 'world-picture') conception of scientific theories as put forth by Toulmin (1963) and Hanson (1963). According to this conception (which he calls the "intellectual fashion" conception[300]),

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[298] Friedman, M. (1974). "Explanation and Scientific Understanding." The Journal of Philosophy **71**(1).

[299] Ibid.

[300] Although he admits this description is rather uncharitable:

> In all fairness, it should be pointed out that most supporters of this account do not believe that the choice of such ideals of intelligibility is completely capricious, depending only on the whims and prejudices of particular scientists. On the contrary, most believe that

explanations produce understanding of a particular phenomenon by relating it to some 'ideal of natural order:'

> At any given time certain phenomena are regarded as somehow self-explanatory or natural. Such phenomena need no explanation. Explanation, within a particular historical tradition, consists in relating other phenomena to such ideals of intelligibility.[301]

As such, what counts as scientific understanding varies with historical tradition, since what counts as an ideal of intelligibility varies as well. A theory that is explanatory – and thus confers understanding – in one tradition may fail to be so in another.

Friedman acknowledges that the intellectual fashion view has historical support,[302] but considers this account of understanding to lack a crucial normative component, as the criteria for a phenomenon's understanding may vary from one

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> these can be good reasons, usually to do with predictive power, for choosing one ideal over another.

Ibid.

[301] Ibid.

[302] One of the most serious challenges to the Standard Model came from the 1962 publication of Thomas Kuhn's *Structure of Scientific Revolutions*. According to Kuhn, all scientific investigations take place within a paradigm, and, thus, cannot sensibly compared to scientific ventures that take place within a different paradigm. Advocates of this approach to scientific explanation hold that theories (and hence the explanations they provide) are relative to the overarching conceptual perspectives in which they are formulated. As a result, philosophers (and other interested parties) should view science as an ongoing social enterprise involving a shared language, methodology, and general worldview. On this account, the philosophical investigation of science involves an analysis of the development, discovery, acceptance and rejection of scientific theories. As such, it is no longer adequate to analyze theories in terms of their rational reconstruction.

paradigm to another. Even though the intellectual fashion account appears to apply to certain episodes in intellectual history:

> However, it seems to me that it would be desirable, if at all possible, to isolate a common, objective sense of explanation which remains constant throughout the history of science; a sense of 'scientific understanding' on which the theories of Newton, Maxwell, Einstein, and Bohr all produce scientific understanding.[303]

Instead, he argues that to derive a fact from any premises whatsoever (be they initial conditions and general laws, as is the case with the Standard Model, or the stated and unstated premises of a particular tradition) is never sufficient, by itself, to render the explanation of a particular phenomenon less mysterious. From his discussion of the three different accounts of scientific explanation, he concludes that a theory of explanation should have three characteristics. First, it should be sufficiently general. Most, if not all scientific theories that we consider to be explanatory should come out as so according to our theory. The theory also needs to be objective, that is, not based on the idiosyncracies of a particular time period (which the intellectual fashion account cannot deliver). Finally, it needs to connect explanation to understanding (where the Standard Model fails).[304]

He argues that our understanding of particular phenomema, and hence our exlanations of these phenomena, involves placing them within a larger cognitive order. He writes:

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[303] Friedman, M. (1974). "Explanation and Scientific Understanding." The Journal of Philosophy **71**(1).

[304] Ibid.

> [T]his is the essence of scientific explanation – science increases our understanding of the world by reducing the total number of independent phenomena that we have to accept as ultimate or given. A world with fewer independent phenomena is, other things equal, more comprehensive than one with more.[305]

But what does it mean to say that a world with fewer independent phenomena is more intelligible than one with more? This question consists of two parts: what it means for a phenomenon to be independent; and what it means for one conception of the world to be more comprehensible than another.

The first part is an issue of ontology, the second epistemology. It is tempting to conceive of the independence of phemonena in terms of causality: if we need not invoke causal processes to explain the phenomena – if they just are – than such phenomena are brute. These phenomena would be the basic laws of physics, the number of stars in the universe, and, in the case of endocrinology, hormones. On this understanding of the independence of the phenomena, a world with fewer such basic facts is more comprehensible than one with more.

While it may be a fact of human cognition that a world with fewer independent phenomena, in the ontological sense, is more comprehensible, there is no guarantee that the ultimate facts of the world are so sparse. One means of avoiding this potentially troublesome ontological commitment is to regard ultimate phenomena as those foundational aspects of our *knowledge*. One can argue that Kitcher's defense of the unification account of understanding through argument patterns takes this approach.

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[305] Ibid.

III. Kitcher's Ideal of Explanatory Unification

Kitcher argues that one of the most important features of a scientific theory is its ability to provide explanations that unify the phenomena. Kitcher argues that we expand our unified picture (and hence increase understanding) by minimizing the number of "brute facts" needed to articulate our scientific theories. A group of phenomena are unified when their explanations can be derived using the same fundamental argument pattern:

> Science advances our understanding of nature by showing us how to derive descriptions of many phenomena, using the same pattern of derivation again and again, and in demonstrating this, it teaches us how to reduce the number of facts that we have to accept as ultimate (or brute).[306]

This, of course, raises the question of what it means for a fact to be "brute." For Kitcher, facts are "brute" in an espistemological sense.

He supports this approach by pointing out that the acceptance of some major scientific research programs depended upon recognizing promises for unifying, and thereby explaining, the phenomena. For example, Newton's universal laws of gravitation used the same pattern of argument to derive (and thereby describe) the orbit of the planets, falling bodies near the surface of the earth, and the tides. This general argument

[306] Kitcher, P. (1989). Explanatory Unification and Causal Structure. Scientific Explanation. P. Kitcher, and Wesley Salmon. Minneapolis, University of Minnesota Press. **XIII:** 410 - 505.

united what had been disparate phenomena under the same general explanation. From his examination of this and other important episodes in the history of science, Kitcher concludes that the notion of an argument pattern is central to that of explanation. To grasp the concept of explanation is to see that if one accepts an argument as explanatory, one is thereby committed to accepting as explanatory other arguments that instantiate the same pattern.[307] The significance of this claim will become apparent in the final chapter. In addition, he claims that we can assess theories (including embryonic theories) by their ability to provide us with such unifying arguments. I discuss this in more detail in what follows.

Kitcher's account relies upon the concept of a 'general argument pattern' consisting of: 1) a schematic argument; 2) a set of sets of filling instructions containing one set of filling instructions for each term of the schematic argument; 3) a classification of the schematic argument.[308]

A sequence of sentences instantiates the general argument pattern just in case it has the same number of terms as the schematic argument of the general argument pattern; each sentence in the sequence is obtained from the corresponding schematic sentence in accordance with the appropriate set of filling instructions; and it is possible to construct a chain of reasoning that assigns to a sentence the status accorded to the corresponding schematic sentence by the classification.

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[307] Kitcher claims that "[t]o grasp the concept of explanation is to see that if one accepts an argument as explanatory, one is thereby committed to accepting as explanatory other arguments which instantiate the same pattern." Kitcher, P. (1998). Explanatory Unification. Introductory Readings in the Philosophy of Science. H. Klemke, and Rudge. Amherst, Prometheus Books**:** 278 - 301.

[308] Ibid.

Scientists ideally aim to 'systematize' the set K of accepted sentences in science by developing one or more argument patterns that can be used to derive some members of K from others. Kitcher defines a systemization of a set of statements as a:

> [C]ollection of derivations, all of whose constituent statements (premises, conclusions, intermediate steps) belong to the set. Each systematization can be seen as instantiating a set of schemata, the basis of the systematization.[309]

In other words, a systematization of a set of statements is a collection of derivations wherein the premises, conclusions, and intermediate steps all belong to the same explanatory set. As such, a systematization is an instantiation of a schema, and explicitly deductive.[310]

Systematizations that are also *explanations* are those with the smallest available set of argument patterns that can be used to infer the largest number of sentences that we accept. This minimal set is the explanatory store E(K). Kitcher's general challenge is that of specifying E(K), the explanatory store over K, which is the set of arguments acceptable as the basis for acts of explanation by those whose beliefs are exactly the members of K. These systematizations need not specify every detail surrounding the emergence of a phenomenon, but can be idealizations or even "explanation-sketches."

The most relevant historical example for my purposes is that of Darwinian evolutionary theory as presented in the *Origin*, which promised to unify a host of biological phenomena. Because he had not worked out the details of his theory, Darwin

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[309] Kitcher, P. (1993). The Advancement of Science: Science Without Legend, Objectivity Without Illusions. New York, Oxford University Press.

[310] Ibid.

could not provide in-depth evolutionary stories. Instead, he offered sketches of selectionist explanations, which Kitcher schematizes as follows:

SIMPLE INDIVIDUAL SELECTION

Question: Why do (virtually) all members of G have [property] P?

Answer:

(1) Among the ancestors of G there was a subgroup of contemporaneous organisms, G_0, such that

(i) a small number of members of G_0 has P;

(ii) none of the members of the generation ancestral to G_0 had P;

(iii) each of the other members of G_0 had one of the variant characteristics $P_1, \ldots, P_n$;

(iv) no other variant of P is present in any generation of the G_0 – G lineage.

(2) Analysis of the ecological conditions and the physiological effects on their bearers of P, $P_1, \ldots, P_n$

Showing

(3) Organisms with P had higher expected reproductive success than organisms with P_1 ($1 \geq i \geq n$)

(4) P, $P_1, \ldots, P_n$ are heritable.

Therefore

(5) P increased in frequency in each generation of the lineage leading from G_0 to G.

(6) There are sufficiently many generations between G_0 and G

Therefore

(7) (Virtually) all members of G have P.[311]

[311] Ibid.

The filling instructions instructions for this schema are as follows: P is to be replaced by the name of a trait; G and G_0 by the names of groups of organisms (populations, species, taxa, etc.). According to the classification of this schema, (1) – (4) are premises leading to (5) using the principle of reproductive fitness. In turn, (5) and (6) act as premises which, using mathematical induction on lineages, leads to conclusion (7).

This schematic sketch of Darwin's argument can be further abstracted:

Initial conditions $C_1, \ldots, C_n$
Generalities $G_1, \ldots, G_m$
Therefore
Present state of affairs.

Where, according to the ideal of explanatory unification, generalities $G_1, \ldots, G_m$ should unify the phenomena. This highly abstracted version of Kitcherian schemata serves as a mere template, with the conditions and laws to be filled in according to the particular scientific field.

Kitcher, in his early writings on unification, explicitly disavows reliance on laws as a part of his attempt to analyze explanation. He claims that *argument patterns*, not laws, are fundamental to scientific explanations. Laws are not what gives science its generality – this is done by the repeated use of a limited number of argument patterns. (This reflects the explicitly deductive nature of Kitcher's account of explanation and, as we shall see later, his hesitation to invoke the notion of causality.) However, Schoonhoven claims that a robust notion of law can be recovered Kitcher's unification account. Kitcher does not deny that there are laws; he merely assigns them a different

provenance and status in his account then that of the earlier deductive-nomological (D-N) model. Kitcher argues that generalizations do not figure in explanations because they are laws, rather, they are laws because they figure in explanations.[312]

It seems clear that on Kitcher's account there are some generalizations that function in argument patterns in much the same way that laws do in the older D-N account. Schoonhoven claims that these general explanatory patterns "bring laws in their wake."[313]

As we have seen, the main logical tool Kitcher uses is that of deductive inference. (He has, on occasion, called himself a "deductive chauvinist.") This has led the ideal of explanatory unification, like the standard model before it, to be accused of ignoring issues of causality. Before I explore this, I demonstrate how the organization/activation model accords with Kitcher's explanatory ideal.

IV. The Organization/Activation Model as an Exemplar of Unification

One of the primary reasons for the rapid acceptance of the organization/activation model, besides providing a crucial resolution to the problem of homosexuality, was its unifying aspects. In their gloss on the effects of the organization/activation hypothesis on the field of behavioral endocrinology, Breedlove and Hampson write:

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[312] Kitcher, P. (1989). Explanatory Unification and Causal Structure. Scientific Explanation. P. Kitcher, and Wesley Salmon. Minneapolis, University of Minnesota Press. **XIII:** 410 - 505.

[313] Schoonhoven, p. ?

> The organizational hypothesis had an immediate and profound effect upon the field of behavioral endocrinology. Many researchers tried to see whether other sex differences in adult behavior were determined by early androgen exposure. In each case, the prediction was clear – exposure of young animals to androgen should make their behavior more masculine in adulthood, while the absence of early androgen should result in more feminine (and less masculine) adult behavior . . . Although there were some interesting exceptions, these predictions were often borne out for many other behaviors.[314]

As mentioned earlier, the general acceptance of the organization/activation model resulted in less attention paid to environmental and genetic factors. As a result of this lack of consideration, most endocrinologists, after the general acceptance of the organization/activation model, were agreed that:

> Sex differences in the hypothalamus are thought to be the basis of sex differences in (1) reproductive behaviour, that is, the menstrual cycle in women, (2) gender identity, that is, the feeling that one is either male or female, and (3) sexual orientation, that is, homosexuality and heterosexuality.[315]

Sex differences in the hypothalamus (and in the brain in general) are, according to the organization/activation model, due to early hormone exposure. This general explanatory model, like Darwin's theory of descent with selection, can be framed in terms of a general explanation sketch:

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[314] Breedlove, S. M., and Hampson, Elizabeth (2002). Sexual Differentiation of the Brain and Behavior. Behavioral Endocrinology. B. Becker, Crews and McCarthy. Cambridge, MIT Press.

[315] Swaab, D., and Hofman, Michel (1995). "Sexual Differentiation of the Human Hypothalamus in Relation to Gender and Sexual Orientation." Trends in Neurosciences **18**(6): 264 - 270.

Question:

Why do (virtually) all members of M with G have P?

Answer:

(1) Among the members of M, when in an embryonic state

(i) Approximately half of the members possess G1

(ii) Approximately the other half possess G2

(2) The possession of G (usually) results in the excretion of H

(i) The possession of G1 (usually) results in the excretion of substance H1

(ii) The possession of G2 (usually) results in the excretion of substance H2

(3) The presence of substance H results in the development of property P

(i) The presence of substance H1 leads to the development of property P1

(ii) The presence of substance H2 leads to the development of property P2

Therefore,

(4) (Virtually) all members of M with G have P

Filling instructions:

M = mammals (all mammals, or just a specific species)

G = gonads

H = hormones

P = sex dimorphic properties

Classification:

(1) – (3) are premises

(4) the conclusion

Thus, in terms of general structure, the organization/activation model, like Darwin's account of evolution, serves as an exemplar for unification.

We can schematize the above argument in terms of the second, more abstract, argument pattern. The initial condition (C1) consist of the presence or absence of fetal

testes, as well as (C2) the presence or absence of external hormonal manipulation. The biological laws consist of (L1) the production of androgens by the fetal testes; (L2) the physiological effects of androgens on the fetus; and (L3) the physiological effects of androgen absence. The argument pattern explaining normal genital development would look something like the following:

NORMAL SEXUAL DEVELOPMENT

(1) Initial conditions:

C1: Presence or absence of testes

C2: No external manipulation

(2) Biological law:

L1: Production of androgens by fetal testes

Therefore:

(3) Hormone production (androgens or lack thereof)

L2: Physiological effects of androgens

(Development of Wolffian ducts; disintegration of Müllerian ducts)

L3: Physiological effects of androgen absence

(Disintegration of Wolffian ducts; development of Müllerian ducts)

Therefore:

(4) Normal male or female genital development.

Importantly for my argument, explanatory models in behavioral endocrinology also fulfill Kitcher's substantive criteria for unifying explanations. In the two historical cases he examines in "Explanatory Unification" – Newtonian mechanics and Darwinian evolutionary theory – he finds three important features:

(i) Prior to the articulation of a theory with high predictive power, certain proposals for theory construction are favored on the grounds of their explanatory promise.
(ii) The explanatory power of embryonic theories is explicitly tied to the notion of unification.
(iii) Particular features of these theories are taken to support their claims to unification.[316]

We can find each of these three features in the organization/activation model. Recall that Phoenix et. al.'s initial reasoning behind their experimental choices was that a finding that prenatal exposure to androgens had an "organizing action" that would influence adult sexual behavior might mean a whole range of adult behavior could be traced (directly or indirectly) to that early exposure. If they could discover the existence of such an organizing action, it:

> [W]ould 1) extend our knowledge of the role of the gonadal hormones in the regulation of sexual behavior by providing information bearing on the action of these hormones or related substances during the prenatal period, 2) be suggestive evidence that the relationship between the neural tissues mediating mating behavior and the morphogenic fetal hormones parallels that between the genital tissues and the same hormones, and 3) direct attention to a possible origin of behavioral differences between the sexes which is *ipso facto* important for psychologic and psychiatric theory.[317]

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[316] Kitcher, P. (1998). Explanatory Unification. Introductory Readings in the Philosophy of Science. H. Klemke, and Rudge. Amherst, Prometheus Books**:** 278 - 301.

[317] Phoenix, C., et. al. (1959). "Organizing Action of Prenatally Administered Testosterone Propionate on the Tissues Mediating Mating Behavior in the Female Guinea Pig." Endocrinology **65**: 369 - 382.

Not only did the proposed model promise to extend knowledge about hormone action, the possibility that it could explain both physiological and behavioral developmental endpoints is specifically cited for its adoption. One of the authors of the 1959 paper, William C. Young, is even more specific about the unifying potential of the postulated model. If, as he predicted, prenatal hormones influenced a wide variety of behaviors, adopting the organization/activation hypothesis would unite:

> [T]he work of experimental embryologists who have concerned themselves so completely with all that is involved in the development and differentiation of the genital tracts, and the work of psychologists and psychiatrists for whom the development and differentiation of neural tissues presents problems of equal interest and importance.[318]

Thus uniting the fields of physiology and behavioral research under the same explanatory model.

Fulfilling the second feature, the explanatory power of the embryonic organization/activation model was indeed explicitly tied to the notion of unification. In his preface to the monograph of a 1963 New England Psychological Association meeting, psychologist John Money *specifically* credits the organization/activation model with creating a new direction for the field of sex research: "It is the new concept of critical periods in the development, however, that has done most to render archaic the dichotomy

[318] Young, W. C. (1961). The Hormones and Mating Behavior. Sex and Internal Secretions. W. C. Young. Baltimore, The Williams and Wilkins Company. **II**.

between physical and psychological."[319] These "critical periods" are specific sorts of hormone exposure during development, rather than learning stages.

When viewed through this endocrinological lens, human behavior, once strictly the province of psychology, came under the rubric of behavioral endocrinology. The appeal of unification has been dramatic: one of the over-arching goals of the field of endocrinology since the seminal 1959 paper has been to refine our understanding of how hormones determine neural organization and how this neural organization determines or influences later behavior. Specifically, physical development (in terms of gross anatomy and neurology[320]) could be explained (primarily) by prenatal hormone exposure, with the

[319] Money, J. (1965). Sex Research: New Developments. New York, Holt, Rinehary and Winston, Inc.

[320] In their extensive review of the principles and mechanisms of sexual differentiation in the vertebrate brain, Cooke et. al. note:

> Perhaps the single most obvious conclusion about sexual differentiation of these neural systems in animals is the pivotal role of steroid hormones. In every case discovered so far, one can manipulate the sexual dimorphism in the nervous system by manipulating steroid hormones.

Cooke, B., et. al. (1998). "Sexual Differentiation of the Vertebrate Brain: Principles and Mechanisms." Frontiers in Neuroendocrinology **19**: 323 - 362.

consequence that the resulting neural structures determine later behavior[321] and cognitive abilities.[322]

Finally, certain features of the model are taken to support its unifying aspects, and these features help to explain the tremendous appeal of the model. In the case of behavioral endocrinology, both general and particular features are taken to support its unifying aspects, which is one of the reasons I consider the organization/activation model to be an exemplar of Kitcherian explanation by unification. One general feature is its ability to explain many aspects of developmental endpoints by appealing to prenatal androgen exposure (or lack thereof). For instance, one textbook author writes:

> In most mammal studies to date, the brain in either sex is feminine until it is converted to a masculine form in males through the action of testosterone. This masculinization, or defeminization, of the brain affects not only sexual behavior

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[321] Raisman and Field, investigating sex dimorphism in the brain, emphasize the importance of early exposure to "organizing" hormones:

> The characteristic sexual differences in the control of gonadotropins and certain aspects of mating behaviour depend not on the genetic sex of the animal but upon whether the brain has been exposed to androgen during a critical perinatal period of development.

Raisman, G., and Field, Pauline (1973). "Sexual Dimorphism in the Neuropil of the Preoptic Area of the Rat and its Dependence on Neonatal Androgen." Brain Research **54**: 1 - 29.

[322] Psychologist Diane Halpern, introducing a chapter on sex-dimorphism in the human brain, writes:

> Not surprisingly, researchers have considered the possibility that sex differences in cognitive abilities may, in part, reflect sex differences in the underlying neural structure or organization of the brain.

Halpern, D. F. (1992). Sex Differences in Cognitive Abilities. Hillsdale, Lawrence Erlbaum Associates.

but also a wide range of behaviors relating to aggression, play, and ingestions, as well as a number of key physiological processes.[323]

Another general feature of the organization/activation model is its ability to explain both typical and atypical developmental outcomes. Specifically, the notion that the prenatal brain acquired gender during a critical period in development could not only explain the sex-dimorphic cognitive and behavioral differences found in "normal" human adults, it also provided a theoretical framework for explaining atypical sex-related behaviors.

One particular feature of the model taken to support its unifying aspects is ability to offer an explanation of the development of homosexuality, considered, by those who disagreed with Beach, to be not just atypical in terms of frequency, but violating norms of sexual development and gendered behavior. (This is discussed in previous chapters.)

V. Criticisms of Unification

Kitcher, in his 1989 work, shies away from invoking causation as a means of resolving traditional problems that beset the Standard Model. More generally, he hesitates to invoke the notion of causality as an element of explanation. He claims that there is "no sense" to the notion of causal relevance except as "that of figuring in the systematization of belief in the limit of scientific inquiry, as guided by the search for

[323] Schulkin, J. (1999). The Neuroendocrine Regulation of Behavior. New York, Cambridge University Press.

unification."[324] Kitcher thus rejects the possibility that there could be some factor, causally relevant to a particular phenomenon K_i, such that no derivation within the explanatory store E(K) could produce a description of K_i using premises which refer to the causally relevant factor. Hence, his "version of the unification approach makes it constitutive of explanatory relevance that there be no basic explanatory (or causal) mechanisms that are not captured in the limits of attempts to systematize our beliefs."[325]

However, Kitcher is more amenable to causation in his later work. In *The Advancement of Science* (1993), he writes:

> Ever since Hume, philosophers have faced the challenge of explaining how we are in a position to gain evidence for statements involving a family of notions – statements that identify causal relationships, statements that talk of objective explanatory dependence, statements that assert that a particular set of objects is a natural kind, statements that talk of natural necessities. The root problem seems to be that we have no semantical account of such statements that will fit into the epistemological account.[326]

Kitcher proposes "strong realism" as a response to the traditional metaphysical and epistemic worries raised by Hume. Without going into details, he claims that strong realists can accept the metaphysical baggage and plausibly claim that the epistemological worries are unfounded.

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[324] Kitcher, P. (1989). Explanatory Unification and Causal Structure. Scientific Explanation. P. Kitcher, and Wesley Salmon. Minneapolis, University of Minnesota Press. **XIII:** 410 - 505.

[325] Ibid.

[326] Kitcher, P. (1993). The Advancement of Science: Science Without Legend, Objectivity Without Illusions. New York, Oxford University Press.

Some reviewers of *The Advancement of Science* were quick to point out that Kitcher had not, in fact, resolved the issues surrounding causality. Richard Miller, for instance, while claiming that Kitcher's ideal of explanatory unification provides a firm basis for the strong realism proposed by Kitcher as the solution to Humean problems, also claims that it cannot provide a *firm enough* basis:

> To begin with, the general equation of warrant with unifying role does not seem to describe well-conducted causal inquiry. Wise historians and psychopathologists are often content with a motely of causal mechanisms even when unification could be improved by some grand scheme.[327]

Miller notes that, given the diverse roles that the notion of explanatory unification can play, one could make the mild claim that it is an important virtue in a field to the extent to which it is rational to expect a minimal set of mechanisms to generate the phenomena. Unfortunately for Kitcher, this mild claim does nothing to support the strong realism he proposes. As mechanistic explanations of phenomena often make use of unobservables, a strong realist would be inclined to accept such unobservables as genuine entities, rather than heuristic devices. However, as Miller points out:

> The mixed record of reliance on literal belief concerning unobservables together with the conceivability of alternative standards of theory choice create a need to vindicate any commitment to unobservables which is more fervent than Mach's belief that theories provide a unified scheme for deducing observable phenomena. An account of causal inquiry is required to fill this need. Yet Kitcher's attempt to

[327] Miller, R. (1995). "The Advancement of Realism." Philosophy and Phenomenological Research **55**(3).

> ground causal inquiry on explanatory unification seems ultimately to support Machian anti-realism, rather than overcoming it.[328]

Kitcher's response to this criticism is that he did account for causality in an adequate fashion. In his "Author's Response," Kitcher claims that Miller's worries are misplaced:

> After arguing that one component of progress consists in identifying correct causal dependencies in nature, I remain officially agnostic between the invocation of mind-independent non-Humean causation in nature, and a Kantian alternative, in which the causal structure of the world is that projected by our explanatory schemata in the limit of our attempts to unify the phenomena.[329]

While Kitcher now includes causal arguments as a part of explanatory unification, he refuses to speculate about the metaphysics of causation. Specifically, he refuses to choose between a strongly realist non-Humean conception of causation and a more moderately realist Kantian one. So it would seem that the later Kitcher has no problem with linking explanatory laws with causal dependencies, even if only for heuristic reasons.

This later, cautious acceptance of causation seems to strengthen the applicability of Kitcher's model to endocrinology. It would allow us to take the intuitively appealing step of talking about how androgen secretions *cause* certain physiological changes. This makes much more sense than strict inferential deduction.

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[328] Ibid.

[329] Kitcher, P. Ibid."Author's Response." 653 - 673.

But I do not think that Kitcher's incorporation of causality into his ideal of explanatory unification solves all the problems. Take, for example, a further instantiation of the argument pattern: the claim that human males are better than females at visuo-spatial tasks because of greater cerebral lateralization. Recall the original schematic argument pattern:

Question:
Why do (virtually) all members of M with G have P?

Answer:
(1) Among the members of M, when in an embryonic state
    (i) Approximately half of the members possess G1
    (ii) Approximately the other half possess G2

(2) The possession of G (usually) results in the excretion of H
    (i) The possession of G1 (usually) results in the excretion of substance H1
    (ii) The possession of G2 (usually) results in the excretion of substance H2

(3) The presence of substance H results in the development of property P
    (i) The presence of substance H1 leads to the development of property P1
    (ii) The presence of substance H2 leads to the development of property P2

Therefore,
(4) (Virtually) all members of M with G have P

Filling this out to instantiate the particular argument about visuo-spatial skills, we get:

Question:

Why do (most) humans who are males possess superior visuo-spatial skills?

Answer:
(1) Among the members of humanity, when in an embryonic state, approximately half possess fetal testes.

(2) The possession of fetal testes (usually) results in the excretion of androgens.

(3) The presence of androgens results in the development of cerebral lateralization

(3') The presence of cerebral lateralization leads to the possession of superior visuo-spatial skills.

Therefore
(4) (Most) humans who are males possess superior visuo-spatial skills.

Even if this is to read as telling a causal story, I find it problematic as an explanation. My main worry is with (3'). While many endocrinologists (and even more psychologists) accept this statement (in Kitcherian terms, it belongs to the set K), the claim that cerebral lateralization *causes* superior visuo-spatial skills is meaningless unless one can explain how the presumed cause actually causes the development of such abilities.

To echo remarks I've made earlier, there are two possible ways of responding to this. One is to point out Kitcher's emphasis upon explanatory promise: although scientists do not yet know the exact details of how cerebral lateralization leads to superior visuo-spatial ability (specifically, why the neural function supporting spatial ability need

to be more lateralized, but functions supporting verbal ability need to be less lateralized), this is merely something that needs to be worked out.

The second response is to point out that explaining a phenomenon by postulating a cause, when one does not know how the cause *causes*, is no explanation at all. One can argue that this is a case of unification without explanation.

In either case, even if Kitcher is willing to admit causes into his explanatory schemata, he needs to be able to explain how the causes cause, in order to be able to 1) support his notion of explanatory promise and 2) avoid "just so" stories.

VI. Conclusion

Because of the Humean problems involved in re-introducing causation into philosophical accounts of scientific explanation, some thinkers – most notably Kitcher – attempt to resolve the problems of causation by excluding it from their account. Instead, scientific explanation confers understanding by unifying the phenomena. The ideal of unification appeals to deeply intuitive desires concerning our overall understanding of the world, intuitive desires fulfilled by the organization/activation model.

In particular, the model was adopted prior to unambiguous empirical support because of its tremendous explanatory promise. This promise – namely, the ability to explain both typical and atypical development – is explicitly one of unification. Like the general Darwinian schema, the organization/activation model can be instantiated to explain a host of phenomena.

While the organization/activation model fulfills all of Kitcher's criteria for explanatory unification, the unificationist ideal cannot account for all aspects of the model's explanatory power. In particular, the model, once accepted, set the stage for investigations into underlying causal pathways. This is the topic of the following chapter.

Chapter 7

Organization/Activation as an Exemplar of Mechanism

I. Introduction

In response to the problems of unification, some writers propose to explain explanation in terms of mechanism. Like unification, mechanism displays the same three virtues that Friedman requires for unification: it is sufficiently general, objective, and connects explanation to understanding. It is general in that the explanatory mechanisms do not need to be limited to the familiar, objective in that what counts as a mechanism does not depend upon the prevailing ideal of natural order, and it connects explanation to understanding in that we understand something when we can explain how it works.

This second, mechanistic, type of understanding involves deducing how things work, and takes a broadly realist approach towards causation.[330] A mechanism is a system of parts that operate or interact like those of a machine, transmitting forces, motion or energy from one part to another. Mechanical systems are organized hierarchically, in that mechanisms at lower levels can produce changes at higher levels.

In the previous chapter, I claim that, initially, the organization/activation model of psychosexual development appears to be a case of explanation by unification. However, a closer examination reveals that the goal of scientists is (and has been) to cash out the initial predictions and explanations of the model in terms of mechanisms. In what follows, I give a brief definition of mechanism and list criteria that distinguish explanatory from non-explanatory models, drawing primarily upon the work of Carl Craver. I then demonstrate how the organization/activation model fulfills these criteria in terms of both the overarching, general methodology, and, more specifically, in terms of investigations into the neurological substrates underlying homosexuality and transsexuality. However, while the model is an exemplar of mechanism in terms of the research program it inspired, the initial appeal and subsequent adoption of the model is due to its explanatory unification.

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[330] E.g., Wilson and Keil, in "The Shadows and Shallows of Explanation" write:

> We take the notion of causation itself to be a primitive notion, one that has its own shadows in both reductive accounts of causation (e.g. Humean accounts) and nonreductive accounts that consider causation to be richer but still analyzable in terms of prior notions (e.g. time, powers, properties).

Wilson, R., and Keil, Frank (2000). The Shadows and Shallows of Explanation. Explanation and Cognition. K. a. Wilson. Cambridge, MIT Press.

II. Definition and Criteria

As is the case in other areas of science, many endocrinologists *explicitly* describe their work as the search for underlying causal mechanisms.[331] In response to the challenges facing the ideal of explanatory unification, some philosophers of science propose to explain explanation in terms of mechanism, wherein we understand something when we can explain the mechanisms that bring that thing about. (Because I am interested in endocrinological explanations of etiologies, I focus on mechanisms that *produce* phenomena, rather than mechanisms that underlie the present functioning of phenomena.)

Most generally, a mechanism is a system of parts that operate or interact like those of a machine, transmitting forces, motion or energy from one part to another. In this sense, a mechanistic description of a phenomenon explains it when that description includes a story about the causes relevant to the phenomenon.

However, the philosophical conception of mechanism and mechanistic explanation incorporates a number of different epistemological and ontological notions – notions that vary over the course of history as well as between particular scientific

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[331] For instance, Morris et. al. begin their review of sexual differentiation by claiming:

> Understanding the mechanisms that give rise to sex differences in the behavior of nonhuman animals may contribute to the understanding of sex differences in humans. In vertebrate model systems, a single factor – the steroid hormone testosterone – accounts for most, and perhaps all, of the known sex differences in neural structure and behavior.

Morris, J., et. al. (2004). "Sexual Differentiation of the Vertebrate Nervous System." Nature Neuroscience **7**(10): 1034 - 1039.

fields.[332] As medical professionals, endocrinologists investigating the causal pathways behind psychosexual developmental endpoints are more concerned with mechanistic *explanations* of the relevant phenomena, as opposed to delineating the underlying ontological categories.

To demonstrate the applicability of the mechanistic account to behavioral endocrinology, I demonstrate how the explanations proffered by endocrinologists satisfy criteria the five requirements listed by Craver in his most recent book on the subject. In addition, these explanations satisfy the criteria required not just for mechanistic models, but also for genuinely explanatory models.[333]

First, mechanistic explanations, in order to fully account for the phenomena they are meant to explain, must begin with an accurate and complete account of those phenomena. For instance, in order to develop an etiological explanation of the development of secondary sex characteristics, endocrinologists must start with an adequate taxonomy of the phenotypes underlying those characteristics.[334] It took many

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[332] In their introduction to the special issue of *Studies in the History and Philosophy of Biology and Biomedical Sciences*, Craver and Darden stress that, historically, the concept of mechanism and mechanistic explanation has varied from time to time and from thinker to thinker:

> For some, the mechanical philosophy is associated primarily with atomism or other varieties of materialism. For some, its central feature is the rejection of teleology and the rejection of explanation via Aristotelian forms. For some, it is associated with mathematical description. For others, it is characterized in terms of a few basic kinds of machines.

Craver, C., and Lindley Darden (2005). "Introduction." Studies in the History and Philosophy of Biology and Biomedical Sciences **36**: 233-244.

[333] Craver, C. (2007). Explaining the Brain: Mechanisms and the Mosaic Unity of Neuroscience. New York, Oxford University Press.

[334] My most up-to-date endocrinology textbook catalogues more than a *dozen* variations of the XX "versus" XY genotypes.

years for scientists to disambiguate the categories of homosexual, transsexual, and hermaphrodite. As scientists investigated the etiologies, these categories became sharpened, which in turn aided the discovery of mechanisms. More generally, it makes common sense that, if one is to explain how a phenomenon comes about, one must start with some sort of definition of that phenomenon.

Second, a complete characterization of the phenomena requires knowing the conditions under which they *fail* to occur, not just standard precipitating conditions. Building endocrine theories of the etiology of sex-dimorphic phenomena requires explaining atypical outcomes, not just typical outcomes. For instance, researchers, after the implementation of tests to determine XX or XY configuration, were surprised to find some individuals who were XY but phenotypically female.[335] The question was to determine under what conditions the presence of a Y chromosome does not result in a male phenotype. Later research discovered two conditions under which the development of a male phenotype failed to occur: a mutation of the SRY region (sex determining region of the Y chromosome) that renders it inactive thus abrogating the process of phenotypic masculinization, and complete androgen insensitivity syndrome (CAIS), wherein the fetal testes produce testosterone, but the body's tissues fail to respond to it.[336]

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[335] There also exist individuals who possess the XX genotype yet are phenotypically male. The sex determining region of the Y chromosome (that which encodes for the production of Sertoli cells, causing a chain reaction that usually results in the male phenotype) is located on the very top part of the short arm of the Y chromosome. As such, it is quite susceptible to the genetic phenomenon of "cross-over" – whereby chromosomes exchange genetic information by crossing over (and hence substituting) their arms. (This phenomenon was illuminated by feminist icon Barbara McClintock.)

[336] See, for instance, Bancroft, J., and Niels Skakkebeak (1978). Androgens and Human Sexual Behavior. Symposium on Sex, Hormones and Behaviour, London, Excepta Medica.; Carter, C. S. (2002). Hormonal Influences on Human Sexual Behavior. Behavioral Endocrinology. B. Becker,

Discovering under which conditions phenomena fail to occur helps to fulfill the third requirement. Not only do researchers need to know the conditions under which phenomena fail to occur, they also need to know their modulating conditions. In other words, they must be able to explain know how variations in the background conditions alter the phenomena. The most famous example of this in the history of endocrinology is the long-term research program dedicated to examining the behavioral consequences of prenatal androgen exposure in human genetic females due to a condition known as congenital adrenal hyperplasia (CAH). While the precise background hormonal modulations could be neither controlled nor modulated for ethical reasons, individuals with this condition were considered to be medical models of the modulating effects of androgens.

Because there are only two typical psychosexual developmental outcomes within the field of behavioral endocrinology (as informed by the organization/activation model), any manipulation and/or investigation of modulating conditions involves the creation of non-standard conditions. In contrast with human models, scientists can deliberately create non-standard precipitating conditions in laboratory animals.

Finally:

> The variety of by-products or side-effects of the phenomena can be crucial for distinguishing "how-possibly" from "how-actually" models; for distinguishing explanatory sketches from complete mechanistic models.[337]

Crews and McCarthy. Cambridge, MIT Press.; and Wilson, J. D. (2001). "Androgens, Androgen Receptors, and Male Gender Role Behavior." Hormones and Behavior **40**: 358 - 366.

[337] Craver, unpublished manuscript

Determining "how-possibly" from "how-actually" explanations has been a hallmark of endocrinological research. While endocrinologists have discovered a remarkable number of "how-actually" models,[338] hypotheses about the etiology of homosexuality and transsexuality remain firmly in the realm of the possible. As such, the endocrine model of these phenomena fails to be genuinely explanatory on mechanistic grounds. However, obtaining an explanatory model on this account is clear, if far from simple: discover the mechanisms.

III. Mechanistic Investigations into Neurological Substrates

In the late 1960s, researchers began to discover sex differences in the neural structure of rats. One neural structure in particular, the medial preoptic area, received special attention. Before these discoveries, the belief that early hormone exposure could permanently alter the structure of the brain (and hence behavior) rested on indirect evidence – specifically, behavioral evidence from lab animals. Indirect as this evidence may have been, many scientists viewed it as confirming the organization/activation model, since "the nervous system controls behavior, (barring the existence of spirits or demons), sex differences in behavior imply that there are sex differences in neural structure."[339]

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[338] For instance, the testes determination pathway or the positive gonadotropic feedback loop that supports ovulation.

[339] Breedlove, S. M., and Hampson, Elizabeth (2002). Sexual Differentiation of the Brain and Behavior. Behavioral Endocrinology. B. Becker, Crews and McCarthy. Cambridge, MIT Press. As Craver and Darden point out, historically, one prominent idea associated with the term

The organization/activation model provided the impetus to search for the neurological basis of sexually dimorphic behavior. In their extensive 1998 review of the principles and mechanisms of sexual differentiation of the brain, Cooke et. al. point out that sex differences observed in the behavior of lab animals foreshadowed the discovery of sex dimorphism in brain structure:

> In the wake of Alfred Jost's pioneering work explicating the role of testicular hormones in organizing internal and external genitalia of mammals, Phoenix, Goy, Gerall and Young [1959] suggested an extension of these ideas to the brain. Based on inferences from the behavior of guinea pigs, they proposed that testicular steroids could permanently alter the developing nervous system to make it more likely to display masculine behaviors, and less likely to display feminine behaviors, in adulthood.[340]

This proposal, it may be recalled, contrasted the well-understood short-term effects of hormones with their long-lasting organizational effects. Besides introducing this distinction, Cooke et. al. claim that:

> Perhaps the most important contribution of the organizational hypothesis was to draw attention to the question of why males and females behave differently. After this landmark paper [1959] the question was refined to, "what is different about males and females that causes them to behave differently?" Once this question

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'mechanism' is that they are naturalized: "[O]ne need not appeal to occult objects or properties to explain their working." Craver, C., and Lindley Darden (2005). "Introduction." Studies in the History and Philosophy of Biology and Biomedical Sciences **36**: 233-244.

[340] Cooke, B., et. al. (1998). "Sexual Differentiation of the Vertebrate Brain: Principles and Mechanisms." Frontiers in Neuroendocrinology **19**: 323 - 362.

was posed, the most obvious potential answer was that the brains of males and females were structurally different.[341]

As a result of this shift in emphasis from external factors (learning) to internal ones, scientists promptly began to investigate the possibility of structural differences between male and female brains responsible for sex-dimorphic behavior. The most obvious difference – the presence or absence of the feedback loop responsible for ovulation – had been known for some time, although scientists had not yet determined the exact mechanisms. But because it was not obvious how this related to sex-dimorphic *behavior*, scientists interested in pinpointing the loci of masculine and feminine behavior did not pursue this.

Instead, they looked for other structural differences, with the hope of correlating these structures with specific aspects of sex-dimorphic behavior. They found three general categories of anatomical sexual dimorphism. The first category involves ultrastructural differences in cellular or synaptic organelles. Here, 'ultrastructure' refers to those elements in the brain too small to be observed, even with technological aids. As such, discussions of the ultrastructure invoke the overall *functional* structure of neurons. The second category involves differences in synaptic or dendritic organization. A synapse defines the contact region between two nerve cells, where nerve impulses are transmitted from one cell to another, while a dendrite is the branching process of a neuron that conducts impulses towards the cell.

[341] Ibid.

The final category involves differences in the gross volume of defined cell groups, i.e., size and shape differences in anatomical structures. This is sometimes referred to as 'cytoarchitecture,' and, because it does not invoke "unobservables" (in contrast to studies of ultrastructure), nor suffered the same technological limitations of investigations of synapses and dendrites (at the time), was much more amenable as a method of investgation. As a result, it has been the primary focus of research into the neurological substrates correlated with homosexuality[342] and, as I discuss later, transsexuality.[343]

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[342] In discussing the resurgence of research on sex differences in the 1970s, Geert de Vries and Patricia Boyle note that:

> Sex differences in structures involved in reproduction were typically associated with sex differences in the functions regulated by those structures. Consequently, such sex differences were believed to help solve the question of how brain structure contributes to brain function. For example, sex differences in the medial preoptic area (MPOA), e.g. in the size of certain cell clusters, or in the distribution of certain transmitters, have often been linked to sex differences in male sexual behavior . . . These associations perpetuate the idea that sex differences in the brain generate sex differences in functions regulated by the brain.

De Vries, G. J., and Boyle, Patricia (1998). "Double Duty for Sex Differences in the Brain." Behavioural Brain Research **92**: 205 - 213.

[343] Louis Gooren, in his 1990 review of endocrinological investigations into transsexualism, writes:

> The main regions of the brain involved with the sexual differentiation process are the hypothalamus, the preoptic area and the amygdala. The brain systems underlying sexually dimorphic behavior are in close proximity to those involved in gonadotropin regulation. The organization of the latter in animals also depends upon androgens. Thereofre, in lower animals, differentiation of gonadotropin as cyclic (normal in females) and tonic (normal in males) usually parallels the differentiation of sexually dimorphic behavior. This close association between male/female dichotomy in brain differentiation and tonic/cyclic gonadotropic secretion has become the corner stone on investigations in humans with regard to the functional difference of their "sexual brains."

Gooren, L. (1990). "The Endocrinology of Transsexualism: A Review and Commentary." Psychoneuroendocrinology **15**(1): 3 - 14.

One of the first areas of sexual differentiation to be discovered was in the medial preoptic area, which is just anterior to the hypothalamus in rats (although many researchers consider it to be a part of the hypothalamus). Researchers in the mid to late 1950s discovered, through a combination of lesion and electrical stimulation studies, that the medial preoptic area was involved in regulating the sexual behavior of rats.[344] Beginning in the early 1960's lesion and electrical-stimulation studies of various parts of the continuum between the hypothalamus and the medial preoptic area either reduced or eliminated male mating behavior, but did not induce gonadal atrophy. Some scientists interpreted these results as confirming Phoenix et. al.'s hypothesis that neural structures regulated sexual behavior, not gonadal hormones, and proceeded to study the medial preoptic area.

In what follows, I review the scientific attempts to find the neurological basis for sex-dimorphic behavior. Specifically, I discuss the three categories of neurological sexual dimorphism as they were discovered in the medial preoptic area of the rat. The following subsection details the attempts to apply these discoveries to the human brain.

Two scientists inspired by the above-mentioned lesion and stimulation studies were Lennart Heimer and Knut Larsson, collaborating members of the University of Göteborg's departments of anatomy and psychology, respectively. As a result of the lesion studies in particular, they hypothesized that "the medial preoptic and anterior

[344] Fisher (using electrical stimulation) concludes: "initial findings tentatively implicate the medial preoptic area in maternal behavior, and the lateral preoptic area in sexual behavior." Fisher, A. (1956). ""Maternal and Sexual Behavior Induced by Intracranial Chemical Stimulation." Science **124**(3214): 228 - 229.

hypothalamic regions . . . would seem to be a center for impulses influencing mating behavior."[345]

To test this hypothesis, they induced lesions in every part of the hypothalamus (except the tuberal area, where lesions can impair circulation and the gonadotrophin feedback mechanism) in male rats. They categorized the placement of these lesions as either within the medial preoptic – anterior hypothalamic continuum or outside of it. Within both of these areas, they created two kinds of lesions: small and large, thus creating four test groups. The rats from all of these groups were then placed with receptive females, and their mating behavior observed. Finally, they performed histological examinations of the rats' brains in an attempt to correlate behavioral impairment with the specific size and placement of the lesions.

Heimer and Larrson discovered that large lesions in the medial preoptic area permanently abolished sexual behavior. Even when the rats were injected with testosterone, they failed to mount any females.[346] In contrast, small lesions in this area impaired, but did not permanently eliminate, mating behavior. Of the 42 rats in this group, 19 of them displayed sexual impairment. Injections of testosterone propionate could restore the mating behavior of these sexually impaired rats.[347]

However, within the group of rats that received small lesions in the continuum, Heimer and Larrson found that:

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[345] Heimer, L., and Larrson, Knut (1966). "Impairment of Mating Behavior in Male Rats Following Lesions in the Preoptic-Anterior Hypothalmic Continuum." Brain Research **3**(2): 248 - 263.

[346] Ibid.

[347] Ibid.

> There was not any relationship neither between the location of the lesion within this area and the occurrence of an impairment of sexual behavior, nor between the size of the lesion and the behavior deficit. These results suggest that there is no specific area of the [medial preoptic – anterior hypothalamic] continuum controlling sexual behavior.[348]

However, other results mitigated this seemingly negative finding. Because both large and small lesions in the hypothalamic regions *outside* of the medial preoptic – anterior hypothalamic continuum did not appear to affect mating behavior, Heimer and Larsson conclude:

> It would seem that there exists, within the hypothalamus, besides a mechanism controlling the release of gonadotrophic hormones and thus via the hormonal system indirectly influencing the mating behavior, another neural mechanism which acts with relative independence of the pituitary function.[349]

That is to say, there appeared to be a neural mechanism *other* than that governing the positive or negative feedback loops that influenced sexual behavior. While Heimer and Larsson are not so bold as to claim that this hypothesized mechanism directly influences mating behavior, their study established the possibility of another structural dimorphism besides that of the positive or negative feedback loop.

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[348] Ibid.

[349] Ibid.

This example of the first category of structural dimorphism was suggestive, but it did not reveal the specific area within the continuum responsible for regulating male mating behavior, nor did it shed any light on the mechanisms involved in female mating behavior. However, this finding inspired endocrinologists to investigate this area of the brain more closely.

The next major discovery of sex-dimorphism within the medial preoptic area involved differences of synaptic and dendritic organization. The discoverers, Geoffrey Raisman and Pauline Field, were explicit about locating the cause of sex dimorphic behavior within the neural substrate:

> By investigating the structural organization of those parts of the central nervous system thought to be concerned in reproductive functions we have attempted to establish an anatomical basis for such functional dimorphism.[350]

Because previous studies had shown lesions of the medial preoptic area led to alterations in sexual behavior, Raisman and Field were intrigued by the possibility of sexual differences in the neural organization of this area. They wanted to obtain a finer-grained anatomical knowledge of the medial preoptic area with the hope that it could shed light on the functional dimorphism. To this end, Raisman and Field looked for the possibility of sex dimorphism in the synaptic organization of the preoptic area. The previous studies gave them a place to start:

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[350] Raisman, G., and Field, Pauline (1973). "Sexual Dimorphism in the Neuropil of the Preoptic Area of the Rat and its Dependence on Neonatal Androgen." Ibid. **54**: 1 - 29.

> The characteristic sexual differences in the control of gonadotropins and certain aspects of mating behaviour depend not on the genetic sex of the animal but upon whether the brain has been exposed to androgen during a critical perinatal period of development. This has led to the view that the preoptic area is a specific site for the action of androgen in sexual differentiation.[351]

A preliminary series of experiments focused upon the neuropil of the preoptic area. (A neuropil is a dense feltwork of interwoven cytoplasmic processes of nerve cells – dendrites and axons – and of neuroglial cells – which provide structural and functional support – in the gray matter of the central nervous system). Raisman and Field found that the neuropil in this area has more non-strial (that is, non-amygdaloid) synaptic contacts on dendritic spines in the female than in the male.[352] Combining this information from these previous studies with the view that the preoptic area is a specific site for androgen action in sexual differentiation, Raisman and Field hypothesized that:

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[351] Ibid.

[352] Ibid. They describe their findings as follows:

> In normal females the number of non-amygdaloid synapses on dendritic spines in the preoptic area is higher than in the male. The suggestion that this difference could be related to the ability of the female to maintain a cyclic pattern of gonadotrophin release and/or behavioral oestrus is supported by published work implicating the preoptic area in the control of ovulation and mating behaviour.

Raisman, G., and Field, Pauline (1973). "Sexual Dimorphism in the Neuropil of the Preoptic Area of the Rat and its Dependence on Neonatal Androgen." Brain Research **54**: 1 - 29.

> If such a structural difference is indeed correlated with sexually dimorphic functions such as ovulation, then it too should be determined by the presence or absence of androgens during the first few days after birth in the rat.[353]

To test this hypothesis, Raisman and Field cut the axons projecting from the stria terminalis, a tract of fibers projecting from the amygdala to the preoptic area and the ventromedial nuclei of the tuberal hypothalamus.[354] Their goal was to determine what synapses would survive in the medial preoptic area in the presence (or absence) of androgens.

They used six groups of rats: (1) untreated adult females; (2) adult females treated with testosterone propionate on the 16th day of life (well after the critical period for neural sexual differentiation); (3) adult males castrated at birth; (4) adult females treated with testosterone propionate on the 4th day of life; (5) intact adult males; and (6) males castrated on the 7th day of life. The castrated males were treated (as adults) with estrogen followed by progesterone in order to induce female behavior.

For convenience, Raisman and Field referred to the first three groups as 'cyclic (describing their presumed pattern of gonadotrophin release) and the remaining three groups as 'non-cyclic.'[355] After the test animals had reached adulthood, and their sexual

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[353] Raisman, G., and Field, Pauline (1973). "Sexual Dimorphism in the Neuropil of the Preoptic Area of the Rat and its Dependence on Neonatal Androgen." Brain Research **54**: 1 - 29.

[354] Anatomically, therefore:

> [T]he stria terminalis links the amygdala with the preoptic area and the tuberal hypothalamus, all areas that have been implicated in the control of gonadotrophin release.

Raisman, G., and Field, Pauline (1971). "Sexual Dimorphism in the Preoptic Area of the Rat." Science **173**(3998): pp. 731 - 733.

[355] Raisman, G., and Field, Pauline (1973). "Sexual Dimorphism in the Neuropil of the Preoptic Area of the Rat and its Dependence on Neonatal Androgen." Brain Research **54**: 1 - 29.

responses tested, they took ultrathin sections from both the preoptic area and the ventromedial nucleus of the animals.

Raisman and Field found sexual dimorphism in a specific part of the preoptic area, the part of the preoptic area traversed by the stria terminalis (a tract of fibers that links the amygdala to the preoptic area), which they named the "strial part of the preoptic area."[356] It is a small, mid-dorsal part of the preoptic area, lying just beneath the anterior commissure, and contains prominent bundles of myelinated axons. When sectioned, it is vaguely triangular in shape. Synapses originating from the strial area are located on dendritic shafts, while synapses originating from other areas of the brain are located on dendritic spines.

They classified and counted synapses in this area, finding that normal females had more synapses on dendritic spines and fewer synapses on dendritic shafts than males. (In other words, females had more synapses of a non-strial origin and fewer synapses of strial origin in this area than males.) In contrast, normal males had more synapses on dendritic shafts and fewer synapses on dendritic spines than females (i.e., more synapses of strial origin).[357]

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[356] Ibid.

[357] Raisman and Field created "maps" to correlate the ultrastructural observations with the information gleaned from light microscopy. These maps were based on a classification of axon terminals and other structures. The axon terminals were divided according to their mode of termination on cell bodies, dendritic shafts or spines, and further subdivided into three groups according to the number of dense core vesicles present. Combining the information, they reconstructed two maps, one for the normal male and the other for the normal female. These maps illustrate several features, one of which is a sex-dimorphic region (defined as the area containing more than ten percent of synapses on dendritic spines). This region was significantly larger in females than in males. Ibid.

In addition, and crucially for the organization/activation hypothesis, early androgen manipulation could reverse the sex difference normally seen in adulthood. In normal females, females treated late in life with androgens, and in males castrated at birth and later treated with estrogens and progestins (all of which Raisman and Field labeled 'cyclic'), the number of non-strial spine synapses found in the preoptic area was significantly higher than the non-cyclic groups. Likewise, normal males, castrated females treated early in life with androgens, and males castrated later in life (after the critical period) all displayed a "masculine" synaptic development.[358]

Before Raisman and Field's report, while many scientists accepted Phoenix et. al.'s hypothesis that differences in sexual behavior reflected sex differences in brain structure, it was entirely plausible to argue that the differences in behavior were (merely) the result of *functional* brain differences. That is to say, the behavioral changes seen following early hormone treatments need not imply any specific structural brain changes whatsoever. But, as Gorski makes plain, Raisman and Field's report confirmed that the sex difference in *function* resulted from a sex difference in neural *structure.*

In the case at hand, it appeared that the structural sexual dimorphism found by Raisman and Field was correlated with the functional sexual dimorphism of positive or negative gonadotropic feedback response. While these researchers were not rash enough to suggest that correlation implies causation, this discovery lent credence to the hypothesis that cyclicity or acyclicity (that is, a positive or negative feedback response) could serve as a *functional* marker for masculine or feminine neural structures. (Later research included handedness, certain cognitive skills such as visuo-spatial ability, and a

[358] Ibid.

variety of other traits as such markers.) In addition, this functional marker of "cyclicity" was to play an important role in theories about human neural sexual differentiation, specifically, in terms of distinguishing male from female brains, and hence heterosexual from homosexual brains.[359]

Raisman and Field's report was tremendously influential, in part because it confirmed the prediction of the organization/activation model that early androgen exposure could permanently organize neural structure, not just function. Cooke et. al., for instance, claim that:

> The widely accepted view that the brains of males and females must be structurally different was confirmed by Raisman and Field's [1973] seminal report that female rats had a greater proportion of certain synaptic types in the preoptic area (POA) than did males.[360]

In addition to confirming Phoenix et. al.'s initial hypothesis, Raisman and Field's work opened up exciting new venues in neuroendocrinology. Endocrinologist Melissa Hines writes:

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[359] In his book, The Sexual Brain, Simon LeVay states:

> The discovery of this anatomical dimorphism [in the medial preoptic area] has been an important element in the elucidation of the mechanisms by which the sexual differentiation of the brain comes about.

LeVay, S. (1993). The Sexual Brain. Cambridge, The MIT Press.

[360] Cooke, B., et. al. (1998). "Sexual Differentiation of the Vertebrate Brain: Principles and Mechanisms." Frontiers in Neuroendocrinology **19**: 323 - 362.

> This discovery [by Raisman and Field] revolutionized thought regarding the neural mechanisms involved in sexual differentiation of the brain. There was now growing confidence that the parts of the brain that determined sexual behavior could be identified, that at least some of the neural sex differences underlying behavioral sex differences were structural, and that the neural sex differences and the mechanisms involved in their development could be studied directly.[361]

As such, sex differences in behavior potentially could be correlated sex differences in brain structure. Specifically, Raisman and Field's study opened up the possibility for scientists to trace the causal path from gonadal hormones to brain structure, from brain structure to function, and from brain function to behavior.

This report by Raisman and Field inspired a flurry of other studies into sexual dimorphism in the brain, as it provided a starting point for linking function to structure. In addition, it set up the medial pre-optic area as the anatomical model for sexual dimorphism in the brain. For instance, Randy Nelson, author of the 2005 *Introduction to Behavioral Endocrinology*, writes:

> Since this early [1973] report, more obvious structural sex differences have been reported. Because of its prominent role in the mediation of mating behavior in several species, the preoptic area (POA) of the hypothalamus has received special attention.[362]

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[361] Hines, M. (2004). Brain Gender. New York, Oxford University Press.

[362] Nelson, R. J. (2005). An Introduction to Behavioral Endocrinology. Sunderland, Sinauer Associates.

Much of neuroendocrinology since has been (and continues to be) concerned with connecting functional neurological differences between the sexes to differences in anatomical structure. In addition, the field of behavioral endocrinology aims to connect behavioral to structural differences.

Of the studies inspired by Raisman and Field's findings, the most dramatic results came from a 1978 study by Roger Gorski and his colleagues.[363] By that time, Gorski and his colleagues agreed that:

> The concept of the sexual differentiation of brain function is now well established, particularly with regard to the regulation of gonadotropin secretion, male and female sexual behavior, the regulation of food intake and body weight, and aggressive behavior.[364]

As mentioned earlier, one of the goals of endocrinology at this time was to link function to structure – that is, to find the neural substrates responsible for the sexually dimorphic behavior mentioned above. This general research goal is akin to Robert

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[363] More than a decade later, Gorski writes that, in 1973:

> Raisman and Field published a study of great importance. They reported that at the ultrastructural level there was a significant sex difference in terms of the number of dendritic spine synapses of non-strial origin in the MPOA; females have significantly more of such synapses. Importantly, they demonstrated that the number of synapses followed the "rules of sexual differentiation." That is, males castrated at birth, or females exposed to androgen after the period of sexual differentiation had a large (female-like) number of synapses, whereas androgenized females or males castrated after the period of sexual differentiation had fewer (i.e., the masculine pattern) of synapses of this type.

Gorski, R. A. (1984). "Critical Role for the Medial Preoptic Area in the Sexual Differentiation of the Brain." Progress in Brain Research **61: Sex Differences in the Brain**: 129 - 146.

[364] Gorski, R. A., et. al. (1978). "Evidence for a Morphological Sex Difference Within the Medial Preoptic Area of the Rat Brain." Brain Research **148**(2): 333 - 346.

Cummins' philosophical account of the role of "function-ascribing" statements in science. In his now-classic 1975 article, he provides a schematic reconstruction of function-ascribing statements:

> X functions as a ϕ in S (or the function of X in S is to ϕ) relative to an analytic account A of S's capacity to ψ just in case X is capable of ϕ-ing in S and A appropriately and adequately accounts for S's capacity to ψ by, in part, appealing to the capacity of X to ϕ in S.[365]

In this account of mechanistic explanation, S is a system with the capacity to ψ, while X is a component of system S that has the capacity to ϕ. As such, analytical account A is an explanation of how a system is able to ψ, given its ability to ϕ. In the case of endocrinology, system S is the mammalian organism, X is a hormone, ϕ is the physiological action of the hormone, and ψ is a developmental endpoint.

Notably, Gorski et. al. claim that the concept of the sexual differentiation of brain *function* assumes that:

> Those functions recognized as 'masculine' in the adult are at least partially the result of the action of testicular hormones on the developing brain, which is undifferentiated and/or inherently female. Although this concept of a permanent or organizing action of the hormonal environment on neuronal differentiation and development is of considerable importance to both neuroendocrinology and neuroscience in general, the mechanism of this effect is poorly understood.[366]

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[365] Cummins, R. (1975). "Functional Analysis." Journal of Philosophy **72**: 741-765.
[366] Gorski, R. A., et. al. (1978). "Evidence for a Morphological Sex Difference Within the Medial Preoptic Area of the Rat Brain." Brain Research **148**(2): 333 - 346.

In order to shed some light on this mechanism, Gorski and colleagues carried out an analysis of the possible effects of the prenatal hormone environment on the brain of the adult rat. Describing the preoptic area as "an extensively studied model of sexual differentiation,"[367] they focused on the gross volume of various substructures in the medial preoptic nucleus. (This is the third category of sexual dimorphism mentioned earlier.)

Gorski et. al. conducted two experiments. In the first, adult rats were gonadectomized, than treated with either a combination of estradiol benzoate and progesterone, testosterone, or nothing. The first combination was meant to induce a positive feedback response (cyclicity), testosterone meant to induce a negative feedback response, with the final group acting as a control. The rats were "sacrificed" either two or five to six weeks later, and their brains examined. Gorski et. al. found that:

> These treatments did not affect the sexual dimorphism in the MPON [medial preoptic nucleus] and, in all groups, nuclear volume in the male animals was significantly greater than that of females whether nuclear volume was expressed in absolute terms or relative brain weight.[368]

Thus implying that sexual dimorphism within the medial preoptic area did not depend upon adult hormone levels – reinforcing the importance of critical periods in development. Gorski and his colleagues found the (absolute) volume of the medial

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[367] Ibid.

[368] Ibid.

preoptic area in males to be up to eight times greater than in females.[369] (When calculated relative to brain size, it is up to five times greater.)

The second experiment used 23 rats of both sexes. The females were injected with either large or small amounts of testosterone propionate, or used as controls. The males were either castrated neonatally or used as controls. After they grew to aduldhood, the rats were sacrificed and subjected to histological examination.[370]

The neonatally castrated male rats in this second group displayed a significant reduction in medial preoptic area volume compared to male rats castrated later in life, after the period of sexual differentiation of the brain. In addition, both the neonatally castrated males and the females injected with the large doses of testosterone propionate displayed medial preoptic areas larger than those of control females. Further investigation showed that late-castrated males had a preoptic area larger than any other of the groups in the experiment.[371]

Pulling all of these results together, they concluded:

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[369] Ibid.

[370] Ibid.

[371] Ibid. In his discussion of mechanisms and role functions, Craver claims that the active organization of mechanisms depends upon the spatial and temporal organization of their components:

> The same entities and activities, strung together in different spatial and temporal relations to one another, can yield very different mechanisms. One understands a mechanism by discovering its component entities and activities, and by learning how their activities are spatially and temporally organized.

Craver, C. (2001). "Role Functions, Mechanisms, and Hierarchy." Philosophy of Science **68**(1): 53 - 74. While the organization/activation model is founded upon temporal organization, the activities of the secretions of the ductless glands do not depend upon their physical location within the body.

> The major findings of this present study are that there is a gross morphological sexual dimorphism in the MPON [medial preoptic nucleus] of the rat, a sexual dimorphism which is independent of the hormone environment of the adult, but one that is at least partially determined by the prenatal environment. The fact that volume of the MPON of the neonatally castrated male is not equivalent to that of the female, or that this volume in the androgenized female fails to reach that of the male castrated at weaning, suggests that partial differentiation may occur prenatally, and/or that the volume of the MPON is influenced by the neuronal genome.[372]

Because the density of neurons per unit within this region is greater than that of the surrounding tissue, Gorski and his colleagues considered this to be a nucleus, which they named the 'sexually-dimorphic nucleus of the POA' (SDN-POA).[373]

This sex-dimorphism of the POA "conforms beautifully to both the organizational and the aromatization hypothesis."[374] Not only did castration of males on the day of birth cause their SDN-POAs to be smaller (i.e., less masculine) in adulthood, androgen treatment of newborn females caused their SDN-POAs to be larger in adulthood. Adult hormone manipulations do not alter the volume in either sex. Further investigation showed that the greater the early androgen exposure, the larger the SDN-POA. In addition, prenatal treatment with estradiol produced the same type of masculinizing effect

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[372] Gorski, R. A., et. al. (1978). "Evidence for a Morphological Sex Difference Within the Medial Preoptic Area of the Rat Brain." Brain Research **148**(2): 333 - 346.

[373] Gorski, R. A. (1979). "The Neuroendocrinology of Reproduction: An Overview." Biology of Reproduction **20**(1): 111 - 127.

[374] Cooke, B., et. al. (1998). "Sexual Differentiation of the Vertebrate Brain: Principles and Mechanisms." Frontiers in Neuroendocrinology **19**: 323 - 362.

as did testosterone. For Gorski and his colleagues, this suggested that the sex-dimorphism of the POA was due to prenatal androgens and their metabolites, rather than a "neuronal genome."

It was thought that the sexually-dimorphic nucleus of the preoptic area (SDN-POA) might provide an anatomical signature of androgen's influence upon the rat nervous system, and thus serve as a model for neural sexual differentiation in general. A year after the publication of his 1978[375] report, Gorski, noting that "it would be very helpful if one could identify a clear signature of sexual differentiation upon which appropriate studies could be focused," claims that he and his colleagues "presently believe that we have discovered such a clear signature,"[376] namely, the SDN-POA. Specifically, Gorski and his colleagues found that, in rats, the medial preoptic area was significantly larger in males than in females.

But positing sexual dimorphism in the medial preoptic area as the neural substrate for sexually dimorphic *behavior* is not so easy, as the function of the SDN-POA remains a mystery. To use Craver's terminology, while the SDN-POA served as a how-actually model of androgen's influence upon a specific neural structure, it remained a how-

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[375] Gorski, R. A., et. al. (1978). "Evidence for a Morphological Sex Difference Within the Medial Preoptic Area of the Rat Brain." Brain Research **148**(2): 333 - 346.

[376] Gorski, R. A. (1979). "The Neuroendocrinology of Reproduction: An Overview." Biology of Reproduction **20**(1): 111 - 127. Reflecting upon the decade of studies performed by his research group, Gorski writes:

> We thus submit that the SDN-POA is a morphological signature of the organizational effects of gonadal hormones on the developing brain. Because the magnitude of the sex difference in SDN-POA, we believe this nucleus can serve as a model system to investigate possible mechanisms by which gonadal hormones act to differentiate the brain sexually.

Gorski, R. A. (1984). "Critical Role for the Medial Preoptic Area in the Sexual Differentiation of the Brain." Progress in Brain Research **61: Sex Differences in the Brain**: 129 - 146.

possibly model for sexually dimorphic behavior. In their initial 1978 report, Gorski et. al. caution:

> Although it is tempting to consider that the morphological differences in the MPON may be a reflection of a fundamentally sexually dimorphic function that may be served by these cells, it must be pointed out that the identity of these cells as neurons is not firmly established.[377]

Later research shed no light on the functional significance of the sexually dimorphic area of this region. Researchers following up on Heimer and Larson's work found that destroying the sexually dimorphic area of the hypothalamus in rats of either sex (while sparing the non-dimorphic parts of the medial preoptic area) does not affect their sexual behavior. Specifically, lesions of only this sex-dimorphic area of the POA in females have no effect on their mating cycles or behavior.[378] Likewise, if only the SDN-POA is lesioned in males, they continue to display normal mating patterns, but, in some cases, exhibit temporary or mild impairment.[379]

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[377] Gorski, R. A., et. al. (1978). "Evidence for a Morphological Sex Difference Within the Medial Preoptic Area of the Rat Brain." Brain Research **148**(2): 333 - 346.

[378] Arendash, G., and Roger Gorski (1983). "Effects of Discrete Lesions of the Sexually Dimorphic Nucleus of the Preoptic Area or Other Medial Preoptic Regions on the Sexual Behavior of Male Rats." Brain Research Bulletin **10**(1): 147 - 154.

[379] De Jonge, F., et. al. (1989). "Lesions of the SDN-POA Inhibit Sexual Behavior of Male Wistar Rats." Ibid. **23**(6): 483 - 492. More than a decade later, Cooke et. al. note that:

> The function of the SDN-POA in rats remains disappointingly uncertain. Lesions limited to the SDN portion of the POA have either no discernible effect on behavior, or only a subtle and transient effect on male mating behaviors.

Cooke, B., et. al. (1998). "Sexual Differentiation of the Vertebrate Brain: Principles and Mechanisms." Frontiers in Neuroendocrinology **19**: 323 - 362.

IV. Reaction of the Scientific Community

Except for two not very interesting exceptions (the avian song control system in the zebra finch and androgen-dependent penile spinal reflexes in the male rat) *none* of the three kinds of neuroanatomic differences (ultrastructural, synaptic, and cytoarchitectural) can be correlated with specific sexually differentiated nervous system functions.[380]

In spite of this lack of correlation between the functional and the structural:

> A general hypothesis has been formulated for the mechanism of CNS [central nervous system] sexual differentiation which has much in common with the model for differentiation of the peripheral reproductive tract . . . in mammals, the intrinsic pattern is female, with differentiation towards masculine patterns of gonadotropin secretion and behavior occurring in the male as a result of exposure to testicular hormones during development.[381]

The scientific community, as a whole, quickly accepted this general hypothesis. For instance, just three years aft Gorski et. al. published their 1978 paper, Robert Rubin et. al., in their review of studies attempting to extend the work on lab animals to humans, begin by noting that:

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[380] MacLusky, N. J., and Naftolin, Frederick (1981). "Sexual Differentiation of the Central Nervous System." Science **211**(4488): 1294 - 1303.

[381] Ibid.

> For many sexually dimorphic behaviors (those differing in males and females), it seems necessary that the male CNS be exposed to increased levels of gonadal steroids during early development and that the female not experience this early hormonal stimulation. For some behaviors, this early hormonal exposure is all that appears to be of consequence.[382]

As a result of the aforementioned research, the medial preoptic area became the model for central nervous system masculinization. It was hoped that this model could shed light on the causal, and hence mechanistic, path from the secretion of gonadal hormones to later (particularly adult) behavior.

Roger Gorski, in his 1984 introduction to a special issue of *Progress in Brain Research* dedicated to the relation between structure and function of sex differences in the brain, writes:

> Recent studies of structural sex differences reinforce the importance of the MPOA in the sexual differentiation of the rat brain. This statement does not imply that the MPOA is the only, the principle, or even the most critical site of sexual differentiation. However, the MPOA, or, more precisely, a smaller component of this area [the SDN-POA], does represent a major site of hormone action (presumably direct, although this is yet to be established) and offers a model system for mechanistic studies which heretofore have been impossible.[383]

To this day, endocrinologists (as well as others) consider the sexual dimorphism found in the preoptic area of the rat brain to be the classic model for the influence of

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[382] Rubin, R., et. al. Ibid."Postnatal Gonadal Steroid Effects on Human Behavior." 1318 - 1324.

[383] Gorski, R. A. (1984). "Critical Role for the Medial Preoptic Area in the Sexual Differentiation of the Brain." Progress in Brain Research **61: Sex Differences in the Brain**: 129 - 146.

gonadal hormones on brain structure. Specifically, most scientists now use the medial preoptic area as the general model for sexual dimorphism in the brain. Twenty years after Gorski published the above-quoted article, Cooke et. al. write:

> Perhaps the most widely known animal model for neural sexual dimorphism is found in the rat medial preoptic area (mPOA). The mPOA appears to be a crucial element in reproductive behavior and endocrine status in rats.[384]

Furthermore, the authors of a recent review in the journal *Endocrinology* point out that the work of endocrinologists on animals demonstrates that:

> In mammalian models, a testicular hormonal signal – androgen – masculinizes the developing genitalia and also masculinizes the developing brain. For a wide variety of behaviors, we can arrange for an animal to display either typically male-like or typically female-like behaviors, or something in between, just by manipulating androgen levels at the right time in development. For most behaviors, a single exposure of androgen early in life will masculinize the animal's brain and behavior forever. The rat SDN-POA conformed to this notion beautifully: males deprived of androgen early in life display a small SDN-POA in

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[384] Cooke, B., et. al. (1998). "Sexual Differentiation of the Vertebrate Brain: Principles and Mechanisms." Frontiers in Neuroendocrinology **19**: 323 - 362. In their tremendously influential extension of this model to human beings, Swaab and Hofman note that:

> The sexually dimorphic nucleus of the preoptic area (SDN-POA) of the hypothalamus, as first described in the rat by Gorski and colleagues, is still the most conspicuous morphological sex difference in the mammalian brain.

Swaab, D., and Hofman, Michel (1995). "Sexual Differentiation of the Human Hypothalamus in Relation to Gender and Sexual Orientation." Trends in Neurosciences **18**(6): 264 - 270.

adulthood, whereas females exposed to androgen during the perinatal period will display a large SDN-POA.[385]

In addition to considering the SDN-POA to be an exemplar of androgen's effects on development, and hence an exemplar for the organization/activation model, many scientists use the notion of the preoptic area as the anatomical signature of the organizational effects of androgens as the basis for further hypotheses. These include hypotheses of cerebral lateralization, sex differences in cognitive abilities, and the etiology of homosexuality and transsexuality.

The widespread acceptance of the organization/activation model of neurological development brought with it three foundational assumptions. First, there is a notion of masculine or feminine exemplars: typical brains are either masculine or feminine, and this depends upon early hormone exposure. Second, this neural organization is permanent, and, finally the nature of this organization can be determined by certain aspects of behavior.

V. Application of Neurological Rat Studies to Humans

In spite of the mystery surrounding the function of the SDN-POA, endocrinologists quickly extended this model to humans. The most obvious extension was to the ability or inability to support the positive gonadotropic response that can induce ovulation. While this was used as a functional marker for feminine or masculine

[385] Morris, J., et. al. (2006). "Brain Aromatase: Dyed-in-the-Wool Homosexuality." Endocrinology **145**(2): 475 - 477.

neural development, it was not correlated with sex dimorphic behavior, and so was not extensively studied in and of itself. Instead, researchers used a "two-pronged" approach: finding anatomical correlates to rodent neural structures; and examining the behavior of presumed human correlates to animal models of central nervous system masculinization. As the second prong is discussed in the fourth chapter, the following explores the first prong.

Taking their cue from the work initially done by Phoenix et. al. in 1959, and extending the SDN-POA model to human beings, Dutch endocrinologists Dick Swaab and Michel Hofman claim that:

> In analogy with observations in many mammalian species, the human brain might well undergo sexual differentiation during its development as a result of an organizing effect of sex hormones, and such a structural organization might be the basis for functional sex differences.[386]

Inspired by Raisman and Field's 1973 work on synaptic and dendritic organization, as well as by Gorski et. al.'s discovery of cytoarchitectural sex differences in rats,[387] Swaab and his colleague Fliers looked for a sex difference in the human

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[386] Swaab, D., and Hofman, Michel (1995). "Sexual Differentiation of the Human Hypothalamus in Relation to Gender and Sexual Orientation." Trends in Neurosciences **18**(6): 264 - 270.

[387] While noting that they knew of no reports of sex difference in cell number for any part of the human brain, Swaab and Fliers point out that:

> Since Raisman and Field reported sex differences in the synaptic organization of the preoptic area of the rat, reports pertaining to gender-linked differences in many brain components throughout the animal kingdom have increased. The most conspicuous of these sex differences was described by Gorski et. al. within the rat brain, in the preoptic area (POA).

analogue of the rat SDN-POA. To this end, they examined the hypothamali of cadavers, with an eye towards high cell density and sexual dimorphism that marks the SDN-POA of rats.

After fixing the brains of thirteen men and eighteen women (between the ages of ten and ninety-three) in formalin for approximately a month, they took serial coronal sections from the hypothalamus and stained them. Swaab and Fliers found a sexually dimorphic nucleus in the human POA that, as in the case of rats:

> [W]as characterized by its more intense staining, larger cell bodies, and higher cell density than the rest of the POA. The SDN-POA was located in the medial POA, between the dorsolateral supraoptic nucleus and the rostral pole of the paraventricular nucleus.[388]

Swaab and Fliers measured the shape, volume and cell density of this sexually dimorphic nucleus. Dividing their human subjects into three age groups (10 – 40; 41 – 70; 71 – 100), they found the SDN-POA volumes to be 2.2, 2.0, and 3.3 times larger in men than women, respectively. When the SDN-POA volume was expressed as ratio to brain weight, the values were significantly larger in men than women for all age groups. The total cell number was 1.74, 1.96, and 2.75 times larger in men than women. In addition, the maximum cross-sectional area was 2.1 times as large in men than in women.[389]

Swaab, D., and Fliers, E. (1985). "A Sexually Dimorphic Nucleus in the Human Brain." Science **228**(4703): 1112 - 1115.

[388] Ibid.

[389] Ibid.

Interestingly, Swaab and Fliers found that in both sexes the volume, cell number and maximal cross-sectional area of the SDN-POA decreased with age. While this result had not been observed in animal tests, Swaab and Fliers did *not* assume that the decrease is due to the changing hormonal milieu of adulthood. They did not make this assumption because of one of their test subjects, a forty-six year old woman who had been virilized by a tumor of the adrenal cortex. Her SDN-POA measurements were similar to the other female values, "which is in agreement with Gorski's (1978) data on the rat," namely, that prenatal gonadal hormone exposure determined the size of the POA.[390]

Noting that the function of the SDN-POA "is unknown in both the rat and humans," Swaab and Fliers expressed hope that immunocytochemistry could be a potent technique for continuing study of this area. (Immunocytochemistry is the technique by which an antibody is used to link a cellular antigen to a specific strain of cultured cells, so that the cells can be seen more easily with a microscope.)

In 1989, Laura Allen, along with Melissa Hines, James Shryne and Roger Gorski, inspired by recent technological advances (including immunocytochemistry), continued the project of correlating structural with functional sexual dimorphism. They reported a second discovery of sexual dimorphism in the human brain. Noting that, besides Swaab and Fliers' report, earlier animal studies demonstated various sexual dimorphisms, they concluded that: "Because the POA shows the greatest number of reported gender-related

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[390] Ibid. On the face of it, it is odd that they could be so certain in this assumption on the basis of one test subject.

dimorphisms in other mammalian species, it is a likely site for similar differences in humans."[391] However:

> Since there are no clear boundaries in the human brain between the POA and the anterior hypothalamus, and, in fact, some anatomists consider the POA to be the anterior region of the anterior hypothalamus, we selected the preoptic-anterior hypothalamic area (PO-AHA) for quantitative analysis of possible sexually dimorphic nuclei in the human brain.[392]

To see if this possibility was an actuality, Allen and her colleagues examined the brains of twenty-two human subjects – eleven males and eleven females, all age matched. After fixing the brains in gelatin, taking coronal sections and staining them, Allen et. al. obtained the following results:

> Since we were unable to identify any cell group clearly homologous to a sexually dimorphic nucleus of another species, 4 relatively discrete cell groups within the PO-AHA that stained darkly with thionin were selected for analysis.[393]

Because these discrete groups had not been identified previously, they elected to name them the "Interstitial Nuclei of the Anterior Hypothalamus" (INAH) and number them one to four in a lateral to medial direction. In addition, they analyzed the size of the supraoptic nucleus.

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[391] Allen, L., et. al. (1989). "Two Sexually Dimorphic Cell Groups in the Human Brain." The Journal of Neuroscience **9**(2): 497 - 506.

[392] Ibid.

[393] Ibid.

Upon a quantitative analysis, Allen et. al. found that the INAH-2 and INAH-3 exhibited a significant sexual dimorphism, while the other two nuclei, as well as the supraoptic nucleus, did not. Specifically, they found the INAH-3 to be 2.8 times larger in the male brain than in the female brain, regardless of the age of the subject.[394] Even though the other striking sexual dimorphism, that of the INAH-2, was found to be twice as large in males than in females, it appeared that the varying size of this nucleus was due, at least in part, to the particular age-related hormonal milieu of the subject. Specifically, Allen and colleagues found that the "INAH-2 was 3.7-fold larger in women of child-bearing age than in prepubescent and post-menopausal females."[395]

Thus while the dimorphism in INAH-2 was equivocal and possibly linked to certain age groups, the dimorphism of INAH-3 was dramatic – about three times as large in males than in females – and independent of age. Because the dimorphism of INAH-3 did not appear to be a function of adult, "activational" hormones, the INAH-3 promised to be a human homolog of the rat SDN-POA.

However, Allen and her collegues were careful to note that:

> It is unclear which, if either, of the 2 nuclei we found to be sexually dimorphic in the human brain corresponds to the SDN-POA of the rat. INAH-3 exhibits similarities to the SDN-POA of the rat by virtue of its location between the optic chiasm and the anterior commissure. However, without knowledge of connectivity or neurochemical characteristics of these nuclei, it is difficult to

[394] Ibid.

[395] Ibid.

> assign any as a homolog to a sexually dimorphic nucleus of another mammalian species.[396]

To use Craver's terminology, the sexually dimorphic nuclei discovered by Allen et. al. could act as "how-possibly" models of neurological substrates underlying human sexual and gendered behavior; but they lack the knowledge required to designate either of the nuclei as "how-actually" models. From this evidence (or, more accurately, lack thereof), as well as the evidence that INAH-2 dimorphism is age-dependent, they conclude:

> Since there appears to be more than one sexually dimorphic nucleus in this region [the POA], and there is presently no indication that INAH-1 is homologous to the SDN-POA of the rat, we do not believe that it is appropriate for INAH-1 to be called the SDN-POA, regardless of its potential sexual dimorphism.[397]

Citing the earlier work connecting prenatal gonadal hormones to sex differences in human behavior, Allen et. al. note that, even though they do not know the genomic determinants, environmental factors, and/or hormone levels responsible for the sex differences in INAH-2 and INAH-3, "there is evidence that some facets of human behavior may be influenced by hormone levels during the prenatal period."[398]

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[396] Ibid.

[397] Ibid.

[398] Ibid. In support of this contention, Allen et. al. cite the work of Hines, M. (1982). "Prenatal Gonadal Hormones and Sex Differences in Human Behavior." Psychological Bulletin **92**(1): 56-80. Hines' claims rely exclusively upon the work of Money and his colleagues at the psychohormone unit.

But what about the previous findings by Swaab and Fliers in humans? During the course of Allen et. al.'s study, Swaab and Fliers:

> [R]eported a sexually dimorphic nucleus in the human POA that resembles the INAH-1 in location, size, shape and cell types, and its dramatic decrease in volume with advancing age . . . Although we firmly believe that the nucleus studies by Swaab and Fliers is the same as INAH-1, we can only speculate as to why they determined this nucleus to be 2.5 times larger in the male brain, whereas we found that INAH-1 was only 1.2-fold larger in males than in females, prior to weight adjustment. Most likely, some discrepancy is due to the fact that our subjects were age-matched.[399]

Specifically, because the dimorphism of the INAH-2 appeared to be due to age and post-natal, activational hormones, it was possible that the volume of the INAH-1 is affected in a similar fashion, albeit only be age. Thus, the results of Swaab and Fliers are an artifact of their methodology,[400] and the human homolog of the rat SDN-POA is the INAH-3, not, as suggested by Swaab and Fliers, the INAH-1.

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[399] Allen, L., et. al. (1989). "Two Sexually Dimorphic Cell Groups in the Human Brain." The Journal of Neuroscience **9**(2): 497 - 506.

[400] Although not all endocrinologists are convinced. Morris et. al. note that:

> Unfortunately, neither Gorski's group [i.e., Allen et. al., 1989] nor [Simon] Levay found a sexual dimorphism in INAH-1, failing to replicate Swaab and Fliers' findings, which may represent a matter of statistical power, because the Dutch group have [sic] much larger sample sizes.

Morris, J., et. al. (2006). "Brain Aromatase: Dyed-in-the-Wool Homosexuality." Endocrinology **145**(2): 475 - 477.

In conclusion, Allen et. al note that, while it is difficult to extrapolate from laboratory animals to humans regarding structural, behavioral, or physiological sex differences:

> It is interesting to speculate that factors such as prenatal stress that both feminize and demasculinize sexual behavior, and decrease the volume of the SDN-POA in male rats may, similarly, contribute in human males to homosexuality and a decrease in the volume of the sexually dimorphic INAH; moreover, the INAH are located in a region of the brain influencing sex differences in gonadotrophin secretion which may be altered in some homosexual men.[401]

Allen et. al. specifically refer to Dörner's hypothesis that male homosexuality results from a feminized brain. As a further research program to follow up on the above possibility – that the INAH may serve as an anatomical marker for male homosexuality – Allen et. al. suggest:

> [M]orphological analysis of the brains from humans with different sexual orientations and identities, during different stages of development, and from individuals exposed perinatally to atypical steroid hormones . . . may lead to further deductions concerning the possible influence of sex hormones on the structure and function of the human brain.[402]

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[401] Allen, L., et. al. (1989). "Two Sexually Dimorphic Cell Groups in the Human Brain." The Journal of Neuroscience **9**(2): 497 - 506.

[402] Ibid.

Later scientists took up this task. Following Barraclough and Gorski's 1961 investigations in rats, and Dörner's extension of this study, most (explicitly) claim that it is the *hypothalamus* that becomes either male or female. Specifically, the hypothalamus either can support the positive gonadotropin feedback loop responsible for ovulation, or it cannot.

But it is clear that endocrinologists want to extend the "maleness" or "femaleness" of brains beyond the hypothalamus, for a number of reasons. First, as we have seen in previous chapters, it is not at all clear how structures that support a positive or negative feedback loop are related to sex dimorphic behavior. Second, a number of other areas of the brain, outside of the hypothalamus, have been found to be sexually dimorphic. Finally, the observed sex dimorphism in cognitive abilities, especially verbal and visuo-spatial abilities, suggests to many researchers that the masculinity or femininity of the brain extends beyond the hypothalamus.

One of the most prominent researchers of "global" brain masculinization or femininization interpretation is Simon LeVay.[403] Under this interpretation, the explanatory sketches for the etiology of particular conditions are quite simple, if somewhat sparse. A genetic male, if exposed to the proper level of androgens in *utero*, develops a masculine brain, and, ultimately, masculine cognitive and behavioral traits: good visuo-spatial ability, poor verbal ability, self-identification as male, sexual attraction to females. The inspiration for LeVay's global model comes from Dörner:

[403] LeVay, for instance, titles one of his chapters in *The Sexual Brain* "My Brain I'll Prove the Female."

> Although Dörner's specific theories have not held up well, his basic idea – that homosexuality, like heterosexuality, results at least in part from specific interactions between androgenic sex hormones and the brain during development – is one that I share.[404]

As a result, failure to manifest any of the above mentioned cognitive or behavioral traits can be explained as the result of low levels of androgens in *utero*. Likewise, if a genetic female were to manifest any of these cognitive traits, this can be explained as due to abnormally high levels of androgens in *utero*.

A number of problems arise within this area. The most serious is that the global conceptualization of the model, though widely accepted, has proved incapable of "specification," i.e., detailed mechanisms of sexual differentiation in accordance with the model have not been found. As we have seen, Dörner considered *all* sex-atypical behavior to be a manifestation of neurological "pseudo-hermaphroditism." As a result, the global conceptualization of the organization/activation model can provide an explanatory sketch for both typical and atypical development, but cannot explain the development of different versions of atypical phenomena.[405]

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[404] LeVay, S. (1993). The Sexual Brain. Cambridge, The MIT Press.

[405] For instance, Heino Meyer-Bahlberg, when asked to justify his practice of grouping homosexuals and transsexuals together in his studies, replies:

> In terms of psychological development, there seems to be a wide overlap between homosexual and transsexual individuals, involving largely identical aspects of sex-dimorphic behavior. Since there is only one broad endocrine theory of sex dimorphic behavior, we assume that it would underly [sic] both homosexual and transsexual development, if at all valid for the human case.

Meyer-Bahlburg, H. (1984). "Psychoendocrine Research on Sexual Orientation: Current Status and Future Options." Progress in Brain Research **61**: 375 - 398.

We have, therefore, a case in which a mode of explanation (at a certain level of generality) is accepted in part because it unifies certain phenomena, and yet is not adequate to handling all the cases; it is therefore not explanatory, which is contrary to what Kitcher's account would lead us to expect.

Some researchers take that to imply that the model is mistaken, others that it merely requires more work in order to be applied to cases. Those endocrinologists who think that the organization/activation model requires more work subscribe to the second conceptualization – a 'local' one wherein masculinization (and feminization) can occur in some parts of the brain but not others. The main support of the local interpretation comes from recent anatomical findings, which are explored in detail in the following chapter.

VI. Conclusion

On the face of it, the research program inspired by the organization/activation model fulfills the general criteria for mechanism. Scientists began with functional definitions of the ultrastructure and anatomical descriptions of synaptic and dendrite connections, and built upon them to distinguish defined cell groups. Besides determining conditions of failure for developmental endpoints, researchers investigated the modulating conditions of early androgen exposure. Finally, certain nuclei (the SDN-POA in particular) were and are considered how-actually models of structural hormonal influence, as well as how-possibly functional models underlying sexual and gendered behavior.

However, the research program inspired by the organization/activation model displays several significant deviations from the standard mechanistic account. First, and foremost, the crucial resolution of the "problem" of homosexuality – a resolution that launched approximately a thousand experiments – was (generally) accepted in advance of any convincing empirical evidence. As it stands, current mechanistic accounts of scientific practice and explanation cannot account for this phenomenon. Second, the tradition of research programs attempting to link outward function to physical mechanisms – a hallmark of mechanistic explanations – is curiously reversed in the recent history of behavioral endocrinology. The discovery of physical sexual dimorphisms in the brain led to an inquiry about the function of those dimorphisms. Even though scientists were unable to uncover the functional significance of said dimorphisms, they were upheld as a model of sexual dimorphism in general.

Finally, this general research program is founded upon ill-defined notions of "masculinity" and "femininity." As will become apparent in the following chapter, these vague, yet foundational, notions have confounded not just the research on homosexuality, but also on transsexuality.

Chapter 8

The Etiology of Transsexuality

I. Introduction

In the previous chapters, I claimed that the crucial resolution of the "problem" of homosexuality was a primary reason for the acceptance of the organization/activation model. Besides solving the puzzle of homosexuality, the model had potentially widespread application. The notion that the prenatal brain acquired gender during a critical period in development promised to explain both normal and pathological development. Not only could the organization/activation model explain the etiology of homosexuality, it promised to explain a host of sexual and sex-related phenomena.

One such phenomenon was transsexuality. Transsexuality, even more than homosexuality, is a phenomenon fraught with vagueness, ambiguity, and categorical, definitional, and professional controversy. The scientific literature approaches both homosexuality and transsexuality in one of three ways: in terms of behavior, in terms of a pseudo-natural kind, and in terms of neurological structures. These categories easily overlap: the category of "persons" can explain, if in a limited fashion, some types and aspects of behavior; neurological structures can play the role of "symptoms" for various kinds of people. All three categorizations appear in the literature, often without explicit disambiguation.

Importantly for my argument, the organization/activation model, once it was accepted as an explanation for homosexuality, was immediately and uncritically extended to other phenomena, including transsexuality. Not only was the model to provide foundation for research into transsexuality, it does so to this day.

The extension of the model to transsexuality took it that the very same general mechanism is thought to be responsible: an unusual hormonal milieu in *utero* causes the development of a gendered brain at odds with the genetic sex. Transsexuality, like homosexuality, thus results from a central nervous system pseudohermaphroditism.

The apparently uncritical extension of the model to the phenomenon of transsexuality raises several issues. On the face of it, this extension appears incongruous. The organization/activation model resolved a problem about sexual orientation, namely, explaining the apparent incompatibility of typical physical development and atypical gender preference. Transsexuality is characterized by typical physical development and atypical gender identity. While both these classifications involve sexuality, gender identity and sexual orientation are usually considered orthogonal categories. It is therefore not immediately obvious why the resolution of the problem of homosexuality should also resolve the problem of transsexuality.

Transfer of the organization/activation model to transsexuality was tempting, but doing so created a new issue urgently in need of resolution: once it was argued that transsexuality and homosexuality are two separate phenomena, the same model was being invoked to explain two different developmental outcomes. If no distinct paths from initial conditions to the distinct outcomes could be exhibited, then not only would transsexuality not be explained, but also the organization/activation model itself might cause to be doubted, even in its original domain of application.

In the case of transsexuality, the elucidation of the mechanisms is not just desirable, but urgent, because the same general model is used to explain two different

developmental outcomes. In particular, the model was supposed to explain both typical and atypical outcomes.

Complicating the search for precise mechanisms was the fact that, at the time when researchers began to look at transsexuality per se, there were two competing conceptualizations of the phenomenon. One view considered transsexuality to be a version of homosexuality – in the words of one researcher, transsexuality is an "extreme version of central nervous system pseudohermaphroditism." This conception, drawing upon the organization/activation model, "explains" both typical and atypical (homosexual) development, with transsexuality being a sub-version of homosexuality. The other view considered transsexuality to be a phenomenon distinct from homosexuality, but also due to some form of central nervous system pseudohermaphroditism. On this other conception of transsexuality, the model explains "typical" (i.e., a gender identity and sexual orientation "congruent" with physiology, in addition to identity-incongruent and orientation-incongruent outsomes. Importantly for my argument, both conceptions of transsexuality were (and are) based upon the organization/activation model. One reason for this is because there is only one general model of psychosexual development. If transsexuality is to be considered a biological phenomenon, then any etiological explanation will be structured by the organization/activation model.

Both conceptions face explanatory problems. With the first conception, the problem is most immediate and glaringly incomplete: how to explain how a particular variation of homosexuality comes about? However, the second conception brings to the fore a more general explanatory conundrum: if both homosexuality and transsexuality are

due to central nervous system pseudohermaphroditism, how can this general explanation give insight into the specifics of two developmental endpoints? If scientists are unable to delineate these pathways, this creates serious doubts about the organization/activation model as an explanatory schema. The widespread applicability of the model, initially seen as a strength, could become its greatest weakness.

In spite of these explanatory problems, the organization/activation model was assumed to explain the etiology of transsexuality. There are several reasons for this, some resulting from the history of the field itself, others more broadly cultural. In exploring these reasons, I want to demonstrate several points.

1) Most generally, cultural and scientific confusion about the classification of transsexuality resulted in divergent presuppositions informing different research projects.

2) It is not immediately obvious why the organization/activation model should be applied to transsexuality in the first place.

3) That the organization/activation model was applied uncritically to the phenomenon of transsexuality demonstrates the rhetorical power of crucial resolutions.

Unfortunately, the history of research into transsexuality has a complicated time line. Because of the early categorical confusions surrounding homosexuality and transsexuality, I first give a brief overview of the field before the general acceptance of the organization/activation model.

After an initial historical introduction, I present a history of investigations into and theories about the etiology of transsexuality. The key concept behind this research is that of gender identity – was it is, and how it develops. Like homosexuality, many

behavioral endocrinologists came to believe transsexualism to have a neuroendocrine correlate.

As mentioned above, there were two general conceptions of transsexuality: that it is a variation of homosexuality, and that it is a distinct (and possibly related) phenomenon. These two different conceptions have different implications for the etiology of gender identity. Historically, each of these conceptions map onto one of two elaborated hypotheses about the etiology of gender identity. Like homosexuality before it, there were two elaborated hypotheses concerning the development of gender identity: that it was learned, and that it had a biological basis.

The first hypothesis postulated external factors as the primary cause behind the etiology of gender identity, while the second postulated causes internal to the individual. In the third and fourth sections, I discuss these etiological hypotheses and their implications for the explanatory power of the organization/activation model. I conclude with a more in-depth discussion of classification issues surrounding transsexualism and gender identity.

As many endocrinologists believe the etiology of transsexuality to be similar or identical to that of homosexuality, the same general investigative techniques are used to determine that etiology: studies of hormonal levels and feedback responses, pseudohermaphrodites and sex-dimorphic cognitive abilities and brain structures. But the most celebrated investigation of the etiology of gender identity is a long-term research project focusing on one individual. I discuss this in the final section of this chapter.

The application of the organization/activation model to transsexuality brings with it, by default, the assumption of an important biological factor. However, because of the supremacy of the organization/activation model, that biological factor is conceived of in terms of prenatal hormonal influence. This results in the explanatory problems mentioned earlier. Besides the problems concerning causal pathways, there is a more general problem: it is not clear that the organization/activation model should be applied to transsexuality in the first place.

II. Historical Background

Early researchers did not distinguish sharply between homosexuality, transsexuality, and hermaphroditism. The initial studies of "pseudohermaphrodites," for instance, did not make a distinction between these three categories. It is due primarily to the work of Jost that the mechanisms behind such forms of pseudohermaphroditism became known. While this distinguished pseudohermaphroditism as a separate phenomenon, both homosexuality and transsexuality initially were thought to arise from adult hormone imbalances. Eventually the definitions of these phenomena were sharpened, and the adult hormone imbalance hypothesis invalidated, to be superceded by the organization/activation model.

Before the widespread acceptance of the organization/activation model, Freudian-inspired theories dominated scientific thinking about homosexuality. In this line of thought, transsexuality, like homosexuality, is a learned behavior. After the acceptance

of the organization/activation model, most scientists accepted that sexual orientation has a biological basis. Along the lines of the organization/activation model, it was tempting to suppose that gender identity also has a biological basis. Nonetheless, some scientists (most notably John Money) argued that gender identity – unlike orientation – is learned. However, this hypothesis was not fully articulated until the mid 1960s.

The other elaborated hypothesis – that the development of gender identity has a biological basis – relies upon the conception of transsexuality as a phenomenon distinct from homosexuality. Historically, this conception was articulated before Money's learning theory, although it took some time for the scientific community to accept it. Central to this discussion is the work of Harry Benjamin, an endocrinologist and sexologist working in New York. Unlike many of his peers, Benjamin considered transsexuality to be a phenomenon distinct from homosexuality – a classification that not all scientists accept, even to this day.

There was no research program dedicated to uncovering the etiology of transsexuality until after the crucial resolution of homosexuality. In light of the methodological precept established by Lillie – that one should investigate the atypical in order to understand the typical – this delay is inexplicable. Because transsexuality is more atypical than homosexuality (in terms of numbers as well as cultural intuitions), it would seem that scientists should prioritize the investigation of transsexuality over that of homosexuality. In terms of actual practice, this delay is due in part to the fact that there were (and are) fewer transsexuals than homosexuals, and thus fewer research subjects, and in part to the conceptual confusions mentioned above.

In the mid-1950s, scientists outside of the field of psychoanalysis began to speculate about the origins of gender identity. Because of the categorical confusions and explanatory problems previously mentioned, uncovering the etiology of gender identity would:

1) help resolve the categorical confusion and, in doing so,

2) shed light on the relative contributions of internal versus external influences on sexual and gendered behavior.

All of this presupposes clear notions of masculine and feminine behavior. After all, one must have a conception of what constitutes gendered behavior in order to investigate the causal factors behind said behavior. As discussed in the fourth chapter, Frank Beach was responsible for categorizing and classifying masculine and feminine behavior in laboratory animals. Unfortunately, said categories were (and are) not so clearly defined in human beings. I discuss this issue further on in this chapter. In spite, or perhaps because of, these cultural presuppositions about what constitutes "proper" or "congruent" gendered/sexual behavior, research into transsexuality brings to the fore in an even stronger way their categorical shortcomings than it does (and did) for investigations into the etiology of homosexuality.

While psychologists and psychiatrists for sometime had been aware of individuals who desired to live as a member of the opposite sex, the publicity surrounding the 1952 Christine Jorensen case first brought this phenomenon to the public eye. Prior to this case (in which a former G.I named Georges Jorgensen requested a sex change) the thinking of most physicians in regards to transsexuality was dominated by

psychotherapists heavily influenced by the thought of Sigmund Freud. These psychotherapists considered Freud's theories to be key for understanding any kind of sexual dysphoria.[406]

The history of research into the etiology of transsexuality provides strong support for my main thesis: that the explanatory power of the organization/activation model lies in its ability to explain a host of developmental endpoints. Both classifications of transsexuality – as a version of homosexuality or as a distinct phenomenon – explain it as the result of atypical sexual brain development. As such, both appeal to a Kitcherian sense of unification in their attempt to explain the etiology of transsexualism.

III. Harry Benjamin

While the term "transsexual" has been in use since the early 1920s, it was not until the mid-1950s' that transsexuality as a category distinct from transvestism, hermaphroditism, and homosexuality emerged.[407] The man primarily responsible for

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[406] Bullough, V. (2000). "Transgenderism and the Concept of Gender." The International Journal of Transgenderism **4**(3): 1 - 10. As late as 1970, some medical doctors subscribed to this view. For example, Margolese writes: "Currently, most authorities consider that altered gender role and sexual preference are largely the result of social and psychological factors." Margolese, S. (1970). "Homosexuality: A New Endocrine Correlate." Hormones and Behavior **1**(2): 151-155.

[407] For an instance of the conflation of these categories, see Witschi, E., and Mengert, William (1942). "Endocrine Studies on Human Hermaphrodites and Their Bearing on the Interpretation of Homosexuality." Journal of Clinical Endocrinology **2**(5): 279-286. In contrast to Chapman, A., et. al. (1951). "Pseudohermaphroditism: A Medical, Social and Psychiatric Case Study." Psychosomatic Medicine: Experimental and Clinical Studies **13**(4): 212 - 219.

creating transsexualism as its own diagnostic category was Harry Benjamin, whose initial diagnostic criteria and etiological speculations are discussed in the first section.

Even though psychologists and psychiatrists had been aware of individuals who desired to live as a member of the opposite sex since before the turn of the last century, the actual number of physicians who professionally addressed the topic was vanishingly small. One of the few who did was Harry Benjamin, who had met with patients in his clinic expressing dissatisfaction with their biological sex for several years before the publicity surrounding the Jorgensen case.[408] In the wake of this publicity, Harry Benjamin was asked to write an article on the subject to be presented at the 1953 meeting of the Association for Advancement of Psychotherapy (and published that same year).[409]

In this article, he used the term 'transsexualism' to describe the subjective conviction of belonging to the opposite sex. The subjective notion of belonging, rather

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[408] Benjamin, H. (1953). "Transvestism and Transsexualism." International Journal of Sexology **7**. In his article on Harry Benjamin, Richard Ekins describes Benjamin as "the founding father of contemporary western transsexualism." Ekins, R. (2005). "Science, Politics and Clinical Intervention: Harry Benjamin, Transsexualism and the Problem of Heteronormativity." Sexualities **8**(3): 306 - 328.

[409] In his extensive review of the etiology of transsexuality, Mormont notes:

> The first surgical case (consisting of a complete sex change: operation, hormone administration and post-operative follow-up), performed by a Danish team, received major media attention from the tabloid press. This case involved Georges Jorgensen, a photographer and ex-GI, who went to Denmark for the operation. At the same time, albeit in New York, Benjamin, an endocrinologist and sexologist, published one of the first scientific articles on the subject. In December 1953, during a symposium held by the Association for Advancement of Psychotherapy, Benjamin and Gutheil coined the term 'transsexualism.'

Mormont, M., and Legros, J. (2001). "A Psycho-Endocrinological Overview of Transsexualism." European Journal of Endocrinology **145**: 365 - 376.

than attraction to, the opposite sex is crucial. Although he was not the first researcher to use this term, he was the first to use it in an unambiguous fashion.[410]

As mentioned, early researchers did not distinguish sharply between homosexuality, transsexuality, and hermaphroditism. The studies of "pseudohermaphrodites," for instance, did not distinguish between these three categories. Benjamin was concerned to disambiguate these phenomena. In a later book devoted to the subject, Benjamin writes:

> The transsexual (TS) male or female is deeply unhappy as a member of the sex (or gender) to which he or she was assigned by the anatomical structure of the body, particularly the genitals. To avoid misunderstanding: this has nothing to do with hermaphroditism.[411]

In other words, the mis-match of gendered elements is a mis-match between subject identity and anatomical features, not an ambiguity of the anatomical features themselves. It is due primarily to the work of Jost that the mechanisms behind pseudohermaphroditism became known.

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[410] Ekins points out that, contrary to popular opinion,

> Benjamin did not coin the term 'transsexual', as is sometimes said. Magnus Hirschfeld had done that way back in 1923. Moreover, David Cauldwell had written quite extensively about transsexuals in the late 1940s and early 1950s. However, Hirschfeld had not developed a distinguishable clinical entity of transsexuality and Cauldwell was largely opposed to transsexual [gender reassignment] surgery, which impeded the development of his thought on the topic.

Ekins, R. (2005). "Science, Politics and Clinical Intervention: Harry Benjamin, Transsexualism and the Problem of Heteronormativity." Sexualities **8**(3): 306 - 328.

[411] Benjamin, H. (1999). The Transsexual Phenomenon. Düsseldorf, Symposium Publishing. Originally published by the Julian Press, Inc., New York, 1966.

As a result of Jost's (and Benjamin's) work, the *absence* of hormonal or gonadal irregularities is part of the present-day definitions of both homosexuality (as discussed in the sixth chapter) and transsexuality.[412] Even after this sharpening of categories, transsexuals were often included in the same studies as homosexuals. The reasons for this will be discussed in the following section.

In addition to distinguishing personal gender confusion from biological ambiguity, Benjamin insisted upon separating transsexualism from homosexuality. Claiming that transsexuals, transvestites and homosexuals should be distinguished based upon both their gender identity (an internal factor) as well as choice of sex partners (an external factor), Benjamin points out:

> The transsexual feels himself to be a woman ("trapped in a man's body") and is attracted to men. This makes him a homosexual provided his sex is diagnosed from the state of his body. But he, diagnosing himself in accordance with his female psychological sex, considers his sexual desire for a man to be heterosexual, that is, normal.[413]

This definition of transsexuality – in terms of the feelings of the subject – paints it as a pseudo-natural kind, a category defined in terms of intentions rather than behavior

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[412] In a much later review of the endocrinology of transsexualism, Louis Gooren points out that:

> Most biological investigations of transsexuals have found that there are no abnormalities in chromosomal pattern, in the gonads or genitals, or in circulating, peripheral sex steroid levels that could account for the condition. The very absence of the above-mentioned abnormalities now constitutes an element in the definition of transsexualism.

Gooren, L. (1990). "The Endocrinology of Transsexualism: A Review and Commentary." Psychoneuroendocrinology **15**(1): 3 - 14.

[413] Benjamin, H. (1999). The Transsexual Phenomenon. Düsseldorf, Symposium Publishing.

per se. While this is a radical change from earlier definitions, it should be noted that Benjamin is still relying upon a very old cultural trope: failure to be a paradigm of one's sex is the result of mix of gendered elements.

In spite of this, Benjamin suspected that transsexuality was due to a biological force. Like many during the early-1960s, he was inspired by the organization/activation model of sexual development, even though he rejected the rigid sex and gender categories many thought it implied. Throughout his career, he consistently presents the view that some hidden biological factor could explain the phenomenon of transsexuality.

In his early writings, Benjamin thinks the two possible biological sources for transsexuality are genetic and endocrinological, although at the time of his 1966 book, "no genetic cause has as yet been proved for any transsexual manifestation."[414] Although genetic research had not been promising, "a possible endocrine cause of transsexualism has been investigated in a few cases with great thoroughness. Beyond a few suspicious findings, no definite proof has as yet been found."[415] (This reflects the explanatory promise of hormones.)

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[414] Ibid. Benjamin cites doctors Melicow and Uson's hypothesis of the etiology of transsexuality: a "sex identification gene" breaks off the Y chromosome and attaches to the X. In spite of its weaknesses, Benjamin comments:

> A theory such as that would indeed explain much better than psychological "conditioning" the astonishing depth and the intensity with which a transsexual identifies with the opposite sex. Incidentally, it would also explain the resistance to treatment.

Benjamin, H. (1999). The Transsexual Phenomenon. Düsseldorf, Symposium Publishing.

[415] Benjamin, H. (1999). The Transsexual Phenomenon. Düsseldorf, Symposium Publishing.

Benjamin does not say so explicitly, but he hints that Gorski's work with rats suggests that male-to-female transsexuals have a "feminine hypothalamus."[416] A year later, in a 1967 article, Benjamin summarized his hypothetical thinking as follows:

> Most satisfying to me is a working hypothesis based on the experiments of brain physiologists and psychobiologists . . . Their possible explanation for the transsexual phenomenon would be neuroendocrine in nature . . If something interferes, perhaps an abundance of the mother's estrogen or lack of the neural target organ, this particular center (a hypothalamic brain center) remains female, determining the later sexual behavior and possibly causing gender role disorientation.[417]

While Benjamin's working hypothesis is more subtle than those who consider transsexuality to be a version of homosexuality – it acknowledges different forms of femininity – it assumes the organization/activation hypothesis as the underlying structure. As such, the brains of transsexuals fail to become properly masculinized, but they fail in a different way than the brains of homosexuals.

As pointed out in the fourth chapter, the adoption of the organization/activation model led to sexual classifications becoming more rigid. While Benjamin did accept aspects of the organization/activation model, his embrace of diversity harks back to the tolerance of some of the early pioneers of sexology. Richard Ekins writes:

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[416] Ibid.

[417] Benjamin, H. (1967). "The Transsexual Phenomenon." Transactions of the New York Academy of Sciences **29**: 428 - 430.

> He [Benjamin] is best placed, perhaps, in the sexological tradition of such important figures as August Forel, Havelock Ellis and Magnus Hirschfeld. He is part of what might be called the liberal wing of sexology which was tolerant of sexual variation and diversity.[418]

Although Benjamin, in his articles as well as in his personal practice, distinguished orientation from identity, few of his colleagues did so. This conglobation of categories may explain the divided response to the Christine Jorgensen case by both the public and the scientific community. Even after the publication of Benjamin's article, many physicians considered transsexualism to be a version of homosexuality, and as such a mental pathology. While the *Journal of the American Medical Association* published the medical history (including treatment and surgery) of the case:

> Many physicians were critical of the use of any treatment other than psychotherapy in a condition apparently of a psychopathological nature. This was especially true of psychoanalysts. Other physicians, not too well versed in sex problems, confused transsexualism with homosexuality. "Oh, just another fairy," one commented to me when speaking of the Jorgensen case.[419]

Benjamin's initial (and subsequent) discussions of the diagnosis, etiology, and treatment of transsexuality provoked hostile reactions from a number of psychoanalysts who argued that removing healthy organs at the request of "emotionally disturbed"

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[418] Ekins, R. (2005). "Science, Politics and Clinical Intervention: Harry Benjamin, Transsexualism and the Problem of Heteronormativity." Sexualities **8**(3): 306 - 328.

[419] Benjamin, H. (1999). The Transsexual Phenomenon. Düsseldorf, Symposium Publishing.

patients was unethical and bad medical practice.[420] In addition, an influential report in the *Journal of the American Medical Association*, released the year after Benjamin's initial publication, rejected the distinctions drawn between transsexualism, transvestism and homosexuality. As a consequence of this definitional rejection, the authors argue against sex-change (re-assignment) surgery:

> Although our subjects share certain needs, wishes, and personality characteristics, it would be completely erroneous to conclude from these similarities that they represent a homogenous group. The need for surgery that these persons share does not in itself represent a disease entity but rather a symptomatic expression of many complex and diverse factors.[421]

For these doctors, it is not the case that transsexuality is a version of homosexuality, but rather that it is not a category (a "disease entity") at all. Instead, it is a pathological syndrome with multiple (as yet unknown) causal agents.

But not only did Benjamin separate transsexualism and homosexuality as two different phenomena, he associated "biological normality" with both. While Benjamin's profession as a medical doctor made it almost inevitable that he would frame his discussions in terms of the medical model of disease, he considered neither homosexuality nor transsexualism to be pathologies – of either body or mind.

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[420] See, e.g., Ostow, M. (1953). "Transvestitism." Journal of the American Medical Association **152**: 1553. Gutheil, E. (1954). "The Psychologic Background of Transsexualism and Transvestitism." American Journal of Psychiatry **8**: 231-235. Lukianowicz, D. (1959). "Survey of Various Aspects of Transvestitism." Journal of Nervous and Mental Disorders **128**(1). Northrup, G. (1959). "Transsexualism: Report of a Case." Archives of General Psychiatry **1**: 332-337. Greenberg, N. (1960). "A Study of Transsexualism." Psychiatric Quarterly **34**: 203-235.

[421] Worden, F., and Marsh, James (1955). "Factors in Man Seeking Sex Transformation: A Preliminary Report." Journal of the American Medical Association **157**: 1291-1298.

Specifically, he did not consider transsexualism to be the result of physiological developmental disorders (thus distinguishing it from hermaphroditism) nor from adult endocrine disorders.[422] In addition, he did not view requests for sex-change surgery to be a symptom of mental illness.[423]

Benjamin held this view, in part, as a result of his adoption of Beach's model of sexual behavior (specifically, Beach's emphasis on the diversity of behavior) and Kinsey's model of a continuum of sexual orientation. If sexual behavior and sexual orientation were to be classified along a continuum, Benjamin saw no reason why sexual or gender identity should not also be so classified:

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[422] Mormont writes:

> The first definition of transsexualism dates from 1953, coined by Benjamin who associated biological normality with the conviction of belonging to the opposite sex and the sex reassignment request.

Mormont, M., and Legros, J. (2001). "A Psycho-Endocrinological Overview of Transsexualism." European Journal of Endocrinology **145**: 365 - 376. As noted earlier, this attribution is, technically, incorrect.

[423] In Billings and Urban's critical review of the treatment of transsexualism, they write:

> The first reported sex-change operation took place in Germany in 1931 (Pauley, 1968) but the procedure was not widely known until Christine (George) Jorgensen's much-publicized surgery in Denmark in 1952. The desire to be a member of the opposite sex had previously been viewed in psychoanalytic literature as an undifferentiated perversion. In 1954, however, U.S. endocrinologist Harry Benjamin asserted that Jorgensen's claim that he was a woman trapped within a man's body was indicative of a unique illness distinct from transvestism and homosexuality, perhaps conditioned by endocrine factors, and not amenable to psychotherapy. He named this non-psychopathic sexual disorder "transsexualism."

Billings, D., and Urban, Thomas (1982). "The Socio-Medical Construction of Transsexualism: An Interpretation and Critique." Social Problems **29**(3): 266-282.

> Again, the thought clearly emerges that what we call "sex" is of a very dubious nature and has no accurate scientific meaning. Between "male" and "female," "sex" is a continuum with many "in betweens."[424]

This focus on the ambiguities of sexual classifications reflects the influences of Beach and Kinsey, with their emphasis upon the overall diversity of behavior, rather than the overall "stability" of patterns (as emphasized by Phoenix and his students). Benjamin took this emphasis to liberal, perhaps even radical, conclusions. In the preface to his book, Benjamin claims:

> The more sex is studied in its nature and implications, the more it loses an exact scientific meaning. The anatomical structures, so sacred to many, come nearer and nearer to being dethroned. Only the social and legal significances of sex emerge and remain.[425]

In other words, Benjamin is suspicious of the tendency to "essentialize" various (if not all) aspects of sexuality, in spite of his description of (male-to-female) transsexuals as women trapped in male bodies. As the reactions to the Jorgensen case mentioned earlier suggest, Benjamin, as a member of the liberal wing of sexology, was in the minority.

The tension between the almost post-modern aspects of Benjamin's broad thoughts on sexuality and his classification of transsexuals as a pseudo-natural kind is due, perhaps, to the fact that, no matter how broad-minded he was, he was trained as a

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[424] Benjamin, H. (1999). The Transsexual Phenomenon. Düsseldorf, Symposium Publishing.

[425] Ibid.

medical doctor, and thus inclined to categorize his patients using the medical model of disease.

Benjamin, as a medical doctor, was more interested in treating transsexuals than determining etiology. But this did not mean that he was uninterested in its etiology. Ekins writes:

> However, while Benjamin left it to others and future research to determine what the genetic or endocrine components might be, he was particularly and repeatedly critical of those who argued that transsexualism was entirely a matter of 'nurture' over 'nature.' Institutionalized American psychoanalysis, from the 1940's onwards, increasingly came to emphasize nurture over nature and some American psychoanalysts were in the vanguard of those critical of the Christine Jorgensen reassignment in the early 1950s.[426]

Many endocrinologists who rejected the tenets of psychoanalysis accepted that the etiology of transsexualism might involve biological factors – although very few accepted Benjamin's opinion that the phenomenon was non-pathological. Something must go awry during development. The search for a mechanism was on – although it was not clear whether the mechanism was one of neurological substrates or socialized learning. Historically, Benjamin's belief that transsexuality is a "constitutional" mismatch between gendered elements of the body, and distinct from homosexuality, was superseded by the etiological theory of gender proposed by John Money.

[426] Ekins, R. (2005). "Science, Politics and Clinical Intervention: Harry Benjamin, Transsexualism and the Problem of Heteronormativity." Sexualities **8**(3): 306 - 328.

IV. John Money and the Learning Theory

In the mid-1950s, scientists outside of the field of psychoanalysis began to speculate about the origins of gender identity – in part because of the Jorgensen case. At this time, the primary hypothesis concerning the etiology of gender identity was that it was learned through socialization. Those scientists who adopted the learning theory looked to the work of John Money.

Money was the most vocal and prominent proponent of the learning theory. His research on pseudohermaphrodites demonstrated (he thought) that, while homosexuality may have a biological component, gender identity did not. As mentioned previously, the most important results in support of this claim came from his studies of CAH girls and women, as they acted as the human equivalent of androgenized female laboratory animal models. Specifically, while a larger than average percentage of CAH girls become lesbians as adults, all self-identified as girls and women.[427] His studies on patients with other forms of pseudohermaphroditism – i.e. with ambiguous genitalia – further convinced him that, with early surgery and sufficient parental and social reinforcement, such individuals who adopt a (usually female) gender identity without problem.[428]

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[427] Three years after the publication of Money's first book, he and his colleagues write: "A salient finding concerning sex and eroticism in the present sample of late-treated women with the adrenogenital syndrome is the relatively high incidence of homosexual inclinations." Ehrhardt, A. A., et. al. (1968). "Influence of Androgen and Some Aspects of Sexually Dimorphic Behavior in Women with the Late-Treated Adrenogenital Syndrome." The Johns Hopkins Medical Journal **123**(3): 115 - 122.

[428] Jean Wilson writes:

> [O]n the basis of studies of subjects with a variety of forms of human intersex and/or endocrine abnormalities, it has been the predominant view that human behavior is more complex than that of other species and that human gender identity and gender role

However, his most celebrated case involved a set of identical genetic male twins, one of whose penis was severed during a botched circumcision. Money and the parents decided to raise the twin in question as a girl, and "Joan's" successful adoption of a female identity was cited as proof of the idea that gender identity is due to the sex of rearing.[429] (This case will be discussed in the final section.)

If gender identity is learned, then the phenomenon of transsexualism is an enigma, as it is difficult to explain how males and females, raised as boys and girls respectively, should develop a gender identity at odds with their socialization. For Money, adults whose gender identity does not match their genital identity simply had an extreme version of what Dörner called "central nervous system pseudohermaphroditism." In other words, transsexualism is a version of homosexuality – and thus biologically rooted. Although he nowhere explicitly states that transsexualism is a version of homosexuality, his writings throughout his professional career implicitly equate transsexuality with homosexuality.[430] (Some of his students do make this equation explicitly, as will be

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> behavior are determine primarily, if not exclusively, by psychological and social forces. According to this anthropocentric view, the human species has been emancipated from biological controls so that the hormones that mediate this aspect of sexual behavior in animals do not play a significant role in controlling human behavior.

Wilson, J. D. (1999). "The Role of Androgens in Male Gender Role Behavior." Endocrine Reviews **20**(5).

[429] Money, J. (1975). "Ablatio Penis: Normal Male Infant Sex Reassignment as a Girl." Archives of Sexual Behavior **4**(1): 65-71.

[430] Contrary to Benjamin's exhortations, Money not only conflates transsexuality with homosexuality, he includes transvestitism in the mix:

> Transvestitism, in the majority of its manifestations, cannot be attributed to postpubertal hormonal dysfunction, nor can homosexuality. The majority of such patients cannot be distinguished from normal members of theirs phenotypic sex, according to present-day techniques and standards. On the other side of the coin, hormonal therapy for

discussed shortly.) This neatly explained the phenomenon while preserving the learning theory of gender identity.

But perhaps not so neatly. While classifying transsexuality as a version of homosexuality, on the face of it, appears to resolve the challenge to Money's learning theory, there remains the underlying implication that central nervous system pseudohermaphroditism can influence the development of gender identity. If transsexuality *is* an extreme version of central nervous system pseudohermaphroditism, then the (subjective) conviction of gender identity is, presumably, the result of that pseudohermaphroditism. In the case of transsexuality, it appears that gender identity does have a biological component. Within the classification scheme and general etiology as put forth by Money, the transsexual is akin to the platypus: an entitiy that defies satisfactory classification; one whose etiology is described as due to either learning or prenatal hormonal influences, but not both.

Money identified male transsexualism, the primary focus of research on transsexuality, as a point on the same continuum as effeminate homosexuality and other "feminine" behavior, including non-effeminate homosexuality and transvestism. [431] (As a

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> transvestites, including transsexuals, and for homosexuals, does not change their psychosexual identity and desire.

Money, J. (1965). "Influence of Hormones on Sexual Behavior." Annual Review of Medicine **16**: 67-82.

[431] As I have argued, this conflation of (male) homosexuality with femininity in general reflects a long-standing cultural trope. In his study of maternal birth order and the incidence of epilepsy, homosexuality and mongols [upon first reading this study, I was surprised at the cross-cultural and cross-racial approach to methodology; upon second reading, I was bitterly disappointed] Eliot Slater points out that, given his findings:

> The clinician would expect male homosexuals to be aetiologically a heterogeneous group, including persons of notably feminized constitution with others of more normal make-up who had become homosexual in sexual attitude from social and psychological causes.

side note, many studies, until fairly recently, have distinguished between "effeminate" and "non-effeminate" homosexuals, without out bothering to define the terms.)[432]

In his 1984 commentary on transsexualism, Gooren claims Money's practice of classifying transsexuals as homosexual is a direct result of Dörner's influence:

> Another point of endless confusion in observational studies is the femininity found in male transsexuals and in some male homosexuals on the one hand and the masculinity in female transsexuals and some lesbians on the other hand. This high degree of similarity to an observer without an attempt to investigate their motivation or intention has led researchers (Dörner, 1980) to believe that there exists a continuum from the male transsexual to the very effeminate male homosexual and on the other end of the scale from the masculine lesbian to the female transsexual.[433]

Gooren considers this lack of emphasis on – or even consideration of – intention to be a mistake. Paraphrasing Benjamin, he points out that, while homosexuals enjoy having sex with members of their own sex, transsexuals (before reassignment surgery) do

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Slater, E. (1962). "Birth Order and Maternal Age of Homosexuals." Lancet **1**(7220): 69 - 71.

[432] See, for instance, Raboch, J., and Sipova, I (1974). "Intelligence in Homosexuals, Transsexuals and Hypogonadotropic Eunuchoids." Journal of Sex Research **10**(2): 156 - 161. Some researchers were hesitant to equate uncritically homosexuality with femininity. Acosta, for instance, points out that

> Although a small percentage of male homosexuals do fit the stereotype of an effeminate, high-voiced, and swishing individual, and do in fact see themselves as more feminine than masculine, they seem to be a minority.

Acosta, F. (1975). "Etiology and Treatment of Homosexuality: A Review." Archives of Sexual Behavior **4**(1): 9 - 29.

[433] Gooren, L. (1984). "Sexual Dimorphism and Transsexuality: Clinical Observations." Progress in Brain Research **61**: 399 - 406.

not take pleasure from their genitals, as they are not the organs they desire to have. This, in his view:

> [C]onstitutes the core difference between homosexuality and transsexuality. It is therefore misleading to rely on observation alone, without an in-depth interview regarding the subjective meaning and the intention of the observed behavior.[434]

In other words, investigations into the etiology of transsexuality should focus on the subjective experiences of people, not on their behavior.

In spite of objections like those above, many of Money's students and colleagues followed (and continue to follow)[435] this practice. For instance, Heino Meyer-Balhburg regularly grouped homosexuals and transsexuals together in his studies. When questioned about this practice, he gave three reasons. First, compared to their genital and gonadal sex (before surgical treatment), almost all transsexuals have a homosexual orientation.[436] (Homosexuality here is defined in terms of genetic sex.) Second, retrospective surveys show "significant cross-gender behavior" during childhood in approximately two thirds of adult homosexuals of either gender. Finally, a number of "markedly effeminate" homosexual males become transsexuals in adulthood.[437]

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[434] Ibid.

[435] See, for instance, Zucker, K., et. al. (1997). "Sibling Sex Ratio of Boys with Gender Identity Disorder." Journal of Child Psychiatry **38**(5): 543-551.

[436] That is to say, most (60%) of male-to-female transsexuals are attracted to men, while the vast majority (95%) of female-to-male transsexuals are attracted to women.

[437] See, for instance, Zucker, K., and Green, Richard (1992). "Psychosexual Disorders in Children and Adolescents." Journal of Child Psychology and Psychiatry **33**(1): 107 - 151.; and Zucker, K., et. al. (1997). "Sibling Sex Ratio of Boys with Gender Identity Disorder." Journal of Child Psychiatry **38**(5): 543-551.

In his justification for combining the categories of transsexual and homosexual, Meyer-Bahlburg exemplifies the fundamental ambiguity the notion of a gendered mismatch. The implications of his reasons are worth noting. First, describing the majority of pre-operative transsexuals as "homosexual" implies that gender classification is determined primarily by genetic sex. There is an element of essentialism here: while male-to-female transsexuals may consider themselves to be women, they are "biologically" male. If, for the sake of argument, Money's learning theory were right, Meyer-Balhburg's reasoning could be construed in a less essentialist light: children who (from the researcher's perspective) become transsexuals as adults are, for the most part, properly socialized with a gender identity in accordance with their genetic sex, but, in terms of sexual orientation, are homosexual.

Importantly, Meyer-Balhburg focuses upon behavior, rather than subjective feelings (in contrast to Benjamin). By focusing on behavior, rather than subjective identification, the category of transsexuality, as a distinct phenomenon rather than a variation on homosexuality, disappears.

Second, while Money strongly denied that the formation of gender identity had hormones as its (proximal and distal) cause, he (and Meyer-Balhburg) firmly believed that many other aspects of sexual behavior did. As such, any manifestation of cross gender behavior could be the result of central nervous system pseudohermaphroditism. However, accepting this statement as true *and* as an indicator of future homosexuality carries with it the assumption that (male) homosexuality is defined by certain types of "feminine" behavior – not just attraction to men.

Finally, the claim that a number of "effeminate" homosexuals become transsexuals in adulthood is ambiguous. It could imply that their sexual orientation was formed (and known) before adulthood. On the face of it, this is untenable, as it makes no sense to talk about sexual attraction before the onset of puberty. If, instead, Meyer-Balhburg interprets early cross-gendered behavior as an indication of (future) homosexuality, this is also untenable, as it assumes that cross-gendered behavior is an indication of homosexuality *per se*, and not transsexuality in particular. On a more charitable interpretation, Meyer-Bahlburg could mean to that some effeminate (adult) homosexuals later became transsexual. However, this is also problematic, as it assumes that these effeminate (male) adults are, in fact, homosexuals.

In spite of the ambiguities in his reasons, he concludes that:

> In terms of psychological development, there seems to be a wide overlap between homosexual and transsexual individuals, involving largely identical aspects of sex-dimorphic behavior. Since there is only one broad endocrine theory of sex dimorphic behavior, we assume that it would underly [sic] both homosexual and transsexual development, if at all valid for the human case.[438]

There are two points of interest in this quote. First, all of these arguments are based upon the notion of sex-dimorphic behavior. This, in turn, relies upon the notions of masculine and feminine behavior, notions that are vague, to say the least. While mating behaviors in laboratory animals are classified as either masculine or feminine, such

[438] Meyer-Bahlburg, H. (1984). "Psychoendocrine Research on Sexual Orientation: Current Status and Future Options." Progress in Brain Research **61**: 375 - 398.

classifications become more difficult when applied to a broader (human) behavioral repetoir.[439]

Second, that there is only one general theory of sex-dimorphic behavior – the organization/activation model – entails that this theory should be able to explain all sex-dimorphic behavior, typical and atypical. In short, the same general explanatory scheme explains, amongst other things, the etiology of both transsexuality and homosexuality. As such, developmental endpoints exhibit congruence between gender and sexual elements, or they do not – either typical or atypical.

In response to this, Meyer-Bahlburg notes that there needs to be some additional explanation as to why some individuals become homosexual and others become "homosexual-plus-transsexual."[440] In other words, the general explanatory model is incomplete. However, even if the phenomena are considered to be two distinct developmental endpoints, the explanatory model is still incomplete, as it cannot explain the precise mechanisms behind the specific mismatches of gendered elements.

Other students of Money's also adopted this "continuum" classification of transsexuality when making clinical diagnoses. While some critics charged that

[439] For instance, an early work of two of Money's students, Ehrhardt and Meyer-Balhburg, describe masculine behavior as characterized by preference for outdoor activities, preference for male over female playmates, greater interest in a career than in housewifery, and less interest in "parenting rehearsal such as doll play and baby care." Ehrhardt, A., and Meyer-Bahlburg, Heino (1981). "Effects of Prenatal Sex Hormones on Gender-Related Behavior." Science **211**(20): 1312 - 1318. Interestingly, the criterion of "housewifery" is not included in later works – reflecting changing conceptions of femininity.

[440] Meyer-Bahlburg, H. (1984). "Psychoendocrine Research on Sexual Orientation: Current Status and Future Options." Progress in Brain Research **61**: 375 - 398.

"transsexualism represents a wish, not a diagnosis,"[441] and as such should not even be its own diagnostic category, much less related to homosexuality, others argued that it should be a distinct diagnosis, albeit related to homosexuality. Howard Baker and Richard Green, for instance, assert that:

> Transsexualism is a behavioral phenomenon unique unto itself. We believe that although it is related to other anomalies of sexual orientation and shares features in common with them, it can, nevertheless, be differentiated.[442]

A fundamental assumption behind this line of thought (and, as we have seen, that of Benjamin) is that transsexuality and homosexuality (and any sort of "atypical" psycho-sexual developmental endpoint) are instances of a mis-match between gendered elements. This general notion informed (and informs) the approach to investigating both homosexuality and transsexuality. For instance, quoting a 1862 letter from German lawyer and homosexual rights activist Ulrichs, Meyer-Bahlburg claims that Ulrichs' notion of "*anima muliebris virili corpori innata* (the soul of a woman innate in a male body) has been the concept guiding biological explanations of homosexuality since then."[443] Of course, Meyer-Bahlburg is speaking metaphorically: when it comes to biological research, the "soul" or essence of a woman is a physical, rather than a spiritual,

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[441] Socarides, C. (1970). "Study of the Desire for Sexual Transformation ('Transsexualism"): The Plaster of Paris Man." International Journal of Psycho-Analysis **51**: 341 - 349.

[442] Baker, H., and Green, Richard (1970). "Treatment of Transsexualism." Current Psychiatric Theory **10**.)

[443] Meyer-Bahlburg, H. (1984). "Psychoendocrine Research on Sexual Orientation: Current Status and Future Options." Progress in Brain Research **61**: 375 - 398.

entity. For endocrinologists, naturally, this "essence" is hormones. For instance, in arguing against the hypothesis that the nervous system alone is responsible for individual variation, Louis Berman points out that:

> It had long been accepted in the inorganic world that differences between substances are due to the differences in the chemistry of them. If they were mixtures of more or less similar substances, the differences between them were ascribable to differences in the relative amounts of the components of the mixture. When it was seen that great differences in the physical and mental make-up and reactions could result from a variation in the amount of an internal secretion acting in an organism, the analogy was complete. One could imagine that individuals, like all other combinations in the universe, were mixtures of similar substances; that individuals were different because of the difference in the amount of the substances entering into their composition; and that the most important of these substances were the internal secretions, because they, fundamentally, controlled the production, distribution and consumption of energy.[444]

As we have seen, some of these substances – gonadal hormones – were gendered from the beginning. As such, maleness and femaleness could be explained by male and female hormones, respectively. The vague hypothesis that both homosexuality and

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[444] Berman, L. (1925). "Anthropology and the Endocrine Glands." Scientific Monthly **21**(2): 157 - 165. Berman is not the first person to voice this hypothesis. Sandor Rado describes Krafft-Ebing's 1896 theory of homosexuality:

> Since the peripheral part of the sexual apparatus [the gonads] is of bisexual disposition, this must be true of the central part as well. Thus one must assume that the cerebrum contains male and female centers whose antagonistic action and relative strength determine the individual's sex behavior. Homosexuality results from the victory of the wrong center.

Rado, S. (1940). "A Critical Examination of the Concept of Bisexuality." Psychosomatic Medicine **11**(4): 459 - 467.

transsexuality are the result of mismatched gendered elements acts as a foundational assumption for the current hypothesis that both phenomena are the result of central nervous system pseudohermaphroditism.[445]

This practice (of Money's) was contentious from the start. One commentator, Frank Acosta, notes that, while some researchers regard transsexualism to be at "the extreme end of the homosexual spectrum":

> The overwhelming findings from current research on homosexuality indicate that neither the majority of male homosexuals nor the majority of female homosexuals identify themselves with the opposite sex.[446]

Thus, despite the "femininity" of male-to-female transsexuals (as Meyer-Bahlburg conceives it), it is a *specific* aspect of femininity – sexual attraction to males – that is the defining criterion of male homosexuality.[447] This modular approach to the

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[445] See, for instance, Herbert, J. (2008). "Who Do We Think We Are: The Brain and Gender Identity." Brain **131**(12): 3115 - 3117.

[446] Acosta, F. (1975). "Etiology and Treatment of Homosexuality: A Review." Archives of Sexual Behavior **4**(1): 9 - 29.

[447] Eleanor Maccoby, in her discussion of the multiple meanings attached to the notions of masculinity and femininity, embodies this type of thinking. Her third meaning of masculinity and femininity deals with attraction between the sexes:

> Probably the most essential ingredient in this definition of masculinity and femininity is that the person should not be, or seem to be, homosexual. Men known to be homosexual may be seen as effeminate even if they do not use feminine gestures, dress, or speech factors.

Maccoby, E. (1987). The Varied Meanings of "Masculine" and "Feminine". Masculinity/Femininity: BAsic Perspectives. J. Reinisch, et. al. New York, Oxford University Press. **I:** 227-239.

gendered brain supports the competing elaborated hypothesis about the etiology of gender identity, to be discussed in the following section.

Not all researchers think that this emphasis upon femininity provides insight into the etiology of either homosexuality or transsexualism. In his critical review of Meyer-Bahlburg's psychohormonal surveys, John De Cecco argues that Money and his students tacitly use the folk wisdom that equates male homosexuality with femininity as the basis for their biological theories.[448] Even though it is apparent that not all male homosexuals are feminine in either appearance or behavior, there must be some hidden femininity to account for the orientation towards men. Following Dörner, the hidden femininity lies in the hypothalamus (discussed in the previous chapter). De Cecco, critical of both this underlying assumption and the conceptual vagueness it entails, writes:

> The equation of femininity with male homosexuality is most graphically portrayed in the conceptualization of homosexuality in relation to bisexuality and

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[448] Vern Bullough also notes that folk wisdom has long linked feminine behavior in boys with latent homosexuality, although, unlike De Cecco, he does not consider this to be a conceptual mistake.
Bullough, V. (2000). "Transgenderism and the Concept of Gender." The International Journal of Transgenderism **4**(3): 1 - 10. Several studies confirmed this link, one of the more important being a longitudinal one by Richard Green (1987):

> Green studied fifty feminine boys over a fifteen year time span. The boys were decidedly feminine as toddlers, so much so that their parents sought professional help at the UCLA Center for Gender studies. The boy children consistently cross dressed very early (94 percent by age six), played with dolls, preferred girl playmates, and indicated they wished they have been girls. Approximately 75 percent of the feminine boys became homosexual as adults compared with only one homosexual man in the fifty member control group. Note, however, that not all the effeminate boys became homosexual, which again indicates that there are many variables involved. None them were transvestites or transsexuals although one had flirted with the idea of surgical change.

Bullough, V. (2000). "Transgenderism and the Concept of Gender." The International Journal of Transgenderism **4**(3): 1 - 10.

> transsexuality. My interpretation of this position is that biological femaleness in males is not unlike Krafft-Ebing's (1886/1906) *taint*: If you have just a little of it, you are a bisexual; if you have a lot (i.e., more femininity than masculinity), you're a homosexual; and if you're drowning in it, you are a transsexual.[449]

In spite of such objections, the concept of central nervous system pseudo-hermaphroditism serves as the foundation for explanations of deviations of psychosexual development, regardless of how one conceptualizes transsexuality. To put it in normative terms, male homosexuals and male-to-female transsexuals, in light of this pseudo-hermaphroditism, fail to be biological exemplars of masculinity. Under both conceptualizations, the goal of scientists researching the etiology of transsexualism is to determine which aspect of normal development goes awry.[450]

Because of this, Acosta, like Gooren after him, cautions researchers to sharply distinguish between the two phenomena:

> Critical differences between homosexuals and transsexuals lie in the repeated findings that, unlike homosexuals, transsexuals (1) have a conviction that they

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[449] De Cecco, J. (1987). "Homosexuality's Brief Recovery: From Sickness to Health and Back Again." The Journal of Sex Research **23**(1): 106-129.

[450] Mormont claims that:

> The aetiology of transsexualism remains uncertain in spite of the hypotheses that, for 40 years, have attempted to mark out the factors that interfering with biological, psychological and social processes of the construction of gender will explain the appearance of transsexualism.

Mormont, M., and Legros, J. (2001). "A Psycho-Endocrinological Overview of Transsexualism." European Journal of Endocrinology **145**: 365 - 376.

belong to the opposite sex and (2) have a strong compulsion to behave like and to have the body of the opposite sex, and to be accepted as one of its members.[451]

For those who do not consider transsexuality to be a version of homosexuality, the same broad endocrine theory explains two different phenomena, not just two versions of the same phenomenon. The distinguishing factor between these two appeals to the organization/activation model is the generality versus modularity of the brain's gender acquisition. This is discussed in the final section of this chapter.

The main blow to the learning theory of gender identity came not from definitional issues, but from the discovery of genetic males who, as a result of an enzyme deficiency, did not develop the (external) male phenotype until puberty, and consequently were raised as girls. At the time of puberty, however, most of these individuals adopted a male gender identity. This finding, and others that lead scientists to question the learning theory, will be discussed in the following section.

V. Demise of the Learning Theory

[451] Acosta, F. (1975). "Etiology and Treatment of Homosexuality: A Review." Archives of Sexual Behavior **4**(1): 9 - 29.

In 1974, a team of researchers working in the Dominican Republic reported a form of pseudohermaphroditism previously unknown to the scientific community.[452] In an isolated community, some girls, upon reaching puberty, developed (external) male genitalia and secondary sex features. The team of scientists (lead by Julianne Imperato-McGinley) called in to investigate hypothesized that this phenomenon was the result of improper testosterone metabolism during embryonic development.

In order for external male genitalia to develop *in utero*, testosterone must be converted by the enzyme 5-alpha-reductase to form dihydrotestosterone.[453] The researchers speculated that individuals who experienced this "sex-change" were deficient in this enzyme. However, because the internal genitalia (including the undescended testes) were masculine, androgens secreted by the pituitary gland at puberty caused masculine differentiation. Subsequent testing proved that these individuals were indeed deficient in the reductase enzyme.

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[452] It should be noted that Witschi, in 1942, briefly describes cases that could be incidences of 5-alpha-reductase deficiency, although the mechanisms were completely unknown. Witschi, E., and Mengert, William (1942). "Endocrine Studies on Human Hermaphrodites and Their Bearing on the Interpretation of Homosexuality." Journal of Clinical Endocrinology **2**(5): 279-286.

[453] Imperato-McGinley et. al. note:

> Within the last 10 years, investigators have shown that testosterone may act as a prehormone, that is, in specific androgen-dependent target areas, it is converted by the microsomal enzyme Δ^4-steroid 5-alpha-reductase to form 5-alpha-dihydrotestosterone, a more potent androgen. It has been demonstrated in human fetuses that, at the time of sexual differentiation in utero, dihydrotestosterone formation occurs in the urogenital sinus, urogenital tubercle, and urogenital swellings, but dihydrotestosterone formation does not occur in the Wolffian anlage until after differentiation has occurred.

Imperato-McGinley, J., et. al. (1974). "Steroid 5-alpha-Reductase Deficiency in Man: An Inherited Form of Male Pseudohermaphroditism." Science **186**(4170): 1213-1215. As discussed in Chapter 3, the primary brain "masculinizing" hormone is estradiol, often converted from testosterone by aromatase.

For many behavioral endocrinologists, the most significant finding was not the new form of pseudohermaphroditism, but the fact that affected individuals adopted a male gender identity upon puberty, in some cases marrying women. Imperato-McGinley and her colleagues also found this to be remarkable:

> Psychosexual orientation (postpubertally) is male, and this is of considerable interest, since the sex of rearing in 18 of the affected males was female. Despite the sex of rearing, the affected were able to change gender identity at the time of puberty. They consider themselves as males and have a libido directed towards the opposite sex. Thus, male sex drive appears to be testosterone related and not dihydrotestosterone related, and the sex of rearing as female appears to have a lesser role in the presence of two masculinizing events – testosterone exposure in utero and again at puberty with the development of a male phenotype.[454]

This initial interpretation, focusing on orientation and sex drive, threatened, but did not necessarily invalidate, Money's learning theory. However, Imperato-McGinley and colleagues subsequently changed the focus of their reports to emphasize the development of gender identity over that of sexual orientation, claiming, for instance:

> In a laissez-faire environment, when the sex of rearing is contrary to the testosterone-mediated biological sex, the biological sex prevails if the normal testosterone-induced activation of puberty is permitted to occur. Thus, it appears that the extent of androgen (i.e., testosterone) exposure of the brain *in utero*,

[454] Ibid.

> during the early postnatal period and at puberty has more effect in determining male gender identity than does sex of rearing.[455]

The finding that gender identity appeared to have a neurological substrate threatened the learning theory. If the roots of gender identity *per se* are biological, and, consequently, transsexualism is *not* a version of (biologically determined) homosexuality, then, presumably, a structural neural difference underlies this functional outcome. In other words, a biological substrate for gender identity, distinct from that for sexual orientation, must be present in the mind.[456] This conjecture – that gender identity, like sexual orientation – is organized in the womb serves as the foundation for contemporary research into its etiology.

The effect of this study was electric. Although the initial report conflated gender identity (in Benjamin's sense) with sexual orientation, the very fact that some individuals "switched" genders upon reaching puberty was seen as a serious blow to Money's learning theory,[457] and provided further support for the organization/activation model.

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[455] Imperato-McGinley, J., et. al. (1979). "Male Pseudohermaphroditism Secondary to 17-beta-Hydroxysteroid Dehydrogenase Deficiency: Gender Role Change with Puberty." Journal of Clinical Endocrinology and Metabolism **49**(3): 391 - 395.

[456] Citing Gooren, van Goozen et. al. (1995) state:

> Thus far, no abnormalities have been found in the sexual differentiation of the transsexual as manifested by the chromosomal patterns, the gonads, secondary sex characteristics and hormone levels. Nevertheless, their persistent and compelling feeling of belonging to the opposite sex might have a brain substrate.

van Goozen, S., et. al. (1995). "Gender Differences in Behaviour: Activating Effects of Cross-Sex Hormones." Psychoneuroendocrinology **20**(4): 343 - 363.

[457] Rubin et. al. (1981) report that:

> Imperato-McGinley et. al. [1977 and 1979] described pubertal shifts from female to male gender identity in an interrelated group of male pseudohermaphrodites from two rural

The use of 5-alpha-reductase deficiency to support the biological theory of gender identity etiology has come under attack in recent years for three reasons: many individuals with this deficiency are identified at birth as "guevedoches" (literally, "eggs at twelve") and so are not raised unambiguously as girls; not all affected individuals adopt an unambiguous male identity; and being male in these communities confers a distinct advantage. In other words, the social environment was not laisse faire.

The very fact that there existed (and exist in one of the two other communities discovered to contain 5-alpha-reductase deficient individuals) a local, ontological, category for said individuals indicates that 5-alpha reductase individuals are not raised unambiguously as either male or female. Such individuals have what contemporary endocrinologists would term "ambiguous" genitalia. The fact that these village communities could label individuals with 5-alpha reductase deficiency *from birth* as failing to be exemplars of either masculinity or femininity indicates that the purely

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> communities in the Dominican Republic and inferred that testosterone exposure during the prenatal, perinatal and, especially, pubertal stages of development is the most significant factor in the normal differentiation of male gender identity. In contrast to this hormonal theory, the more widely held contemporary view is that the sex of rearing, as established by early parental and social influences, is the primary determinant of gender identity. [Citing Money 1972 and 1977]

Rubin, R., et. al. (1981). "Postnatal Gonadal Steroid Effects on Human Behavior." Science **211**(4488): 1318 - 1324. In his report on 5-alpha-reductase deficient individuals in Papau-New Guinea, anthropologist Gilbert Herdt notes:

> The Dominican Republic hermaphrodites posed a major challenge to the break-through theory of Money and the Hampsons (1955). They argued that gender identity development is determined by sex assignment and rearing, not by the gonads, a conclusion which Ellis (1945) had exhaustively presaged in the literature on hermaphroditism.

Herdt, G. (1990). "Mistaken Gender: 5-Alpha Reductase Hermaphroditism and Biological Reductionism in Sexual Identity Reconsidered." American Anthropologist **92**(2): 433-446.

dichotomous categories of male versus female are not sufficient to analyze the local ethnological response.[458]

In addition to questions about the clarity of assigned gender, follow-up studies on the original subjects indicate that not all adopted an uncomplicated male gender identity. Later, more in-depth investigations revealed problematic assumptions and methodological errors:

> Imperator-McGinley et. al. stated that adequate post-pubertal psychosexual data were obtained from 18 of the 19 subjects unambiguously raised as girls, and of these 18 subjects, 17 had successfully changed to a male gender identity and 16 to a male gender role. However, two of the 18 subjects were dead at the time of the reports, and, of the 16 living subjects, one maintained a female gender identity and role despite a masculinized phenotype . . . a second continued to dress as a woman although the investigators regarded his gender identity as unambiguously male; a third lived alone in the hills, even though he was reported to have assumed an unambiguous male role.[459]

Because the ethnography and interview data supplied by Imperato-McGinley et. al. are sketchy at best, the claim that males with 5-alpha-reductase deficiency were raised as "normal" girls but then became "normal" men lacks merit.[460] In other words, genetic

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[458] For an in-depth analysis of this issues, see Herdt, G. (1990). "Mistaken Gender: 5-Alpha Reductase Hermaphroditism and Biological Reductionism in Sexual Identity Reconsidered." American Anthropologist **92**(2): 433-446. in which the author analyzes 5-alpha reductase deficiency in both two-sex and three-sex cultural systems.

[459] Rubin, R., et. al. (1981). "Postnatal Gonadal Steroid Effects on Human Behavior." Science **211**(4488): 1318 - 1324.

[460] In spite of their strong conclusions, Imperato-McGinley and colleagues (1979) inform the reader that:

males with 5-alpha-reductase deficiency fail to be exemplars of gender – either male or female.

In addition to the deficiencies of the empirical claims, one can argue that social forces can influence significantly the adoption of a gender identity. Dominican society (and all of the other societies in which 5-alpha-reductase deficiency are found) is highly patriarchal; an intersex or pseudohermaphroditic individual has much to gain and little to lose by adopting a male gender identity.[461]

In spite of these objections, the fact that most of these individuals change gender at the time of puberty is still cited as evidence for the biological theory – of both sexual orientation and gender identity, although more frequently for the latter. This shows (1) the rhetorical power of the organization/activation model and (2) the related assumption that transsexuality is related to homosexuality.

Arguing against Money's learning theory of gender identity, Jean Wilson writes:

> [V]illagers are aware of the existence of the hermaphroditic condition in local villages, even though the ontology of the guevedoche is never described. We are also told that the prepubertal subjects "showed self-concern over their true gender"; between the ages of 7 and 12 anatomical abnormality made them aware that they were "different."

From Herdt, G. (1990). "Mistaken Gender: 5-Alpha Reductase Hermaphroditism and Biological Reductionism in Sexual Identity Reconsidered." American Anthropologist **92**(2): 433-446.

[461] John Money, highly critical of the Dominican Republic study and the threat it posed to his learning theory, points out:

> Male and female role stereotypes are rigidly dichotomous in a rural Latin-American culture. To be a mannish-appearing woman without breasts, without menses, and without fertility is to be unmarriageable in a society where the unmarried daughter is a family and community liability. The common-sense conclusion for all concerned, the priest and other village authorities included, is to endorse and legally accept a change of gender status, provided the individual concerned does not repudiate it.

Money, J. (1981). "The Development of Sexuality and Eroticism in Humankind." The Quarterly Review of Biology **56**(4): 379-404.

> This belief that hormones do not play a role in controlling human gender role behavior persists despite a large body of evidence to the contrary, indicating that androgens play an important role in human male gender identity/behavior. This evidence stems largely from the work of Imperato-McGinley and her colleagues, who documented that genetic males . . . may change gender role behavior to male at or after the time of expected puberty.[462]

If Money's learning theory was to be salvaged, he would have to demonstrate an example of an individual adopting a gender identity at odds with his or her genetic sex – without any complicating factors such as pseudohermaphroditism. Just such a case is discussed in the next section.

VI. The "John/Joan" Case

Not all researchers were convinced by Money's learning theory of gender identity, even before the publication of the Dominican study. One such person was Milton Diamond who, as an upstart graduate student in 1965, published a paper arguing that gender identity results from prenatal hormonal exposure, not post-natal rearing. Because Diamond's paper drew upon widely accepted endocrinology research, and not just a limited set of human "accidents of nature," it provided a challenge to – even if not a definitive argument against – Money's learning theory.

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[462] Wilson, J. D. (1999). "The Role of Androgens in Male Gender Role Behavior." Endocrine Reviews **20**(5).

Diamond argued that pseudo-hermaphroditic children could be, in light of their condition, truly "bi-potential" in terms of psycho-sexual development, but this did not imply that hormonally average children were so. In order to provide evidence for the latter (i.e., Money's learning theory) there would have to exist at least one case of an unambiguously male infant raised to become unambiguously female in terms of gender identity.[463]

In spite of the difference in their professional stature, Diamond's last point stung. The truth of that matter was that none of Money's "successful" gender acquisitions had occurred in non-hermaphroditic or pseudohermaphroditic individuals. Money, in order to conclusively prove his theory, needed a genetically and hormonally normal infant upon which to experiment. The next year, a couple came to Money's Psychohormonal Research Unit at Johns Hopkins University who presented Money with the golden opportunity to conduct just such an experiment. Linda and Frank Reimer, the parents of 16 month-old identical twin boys, faced a predicament. One of their children, at the age of 8 months, had undergone a botched circumcision that completely destroyed his penis.

Money suggested that the child be raised as a girl. After an initial surgery to remove the testes, Money and his colleagues encouraged the parents to dress and treat "Joan" as a girl, with further surgeries and estrogen to follow at the time of puberty.[464]

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[463] Diamond, M. (1965). "A Critical Evaluation of the Ontogeny of Human Sexual Behavior." The Quarterly Review of Biology **40**(2): 147-175.

[464] In a description of the initial interview with the parents written over ten years later, Money writes:

> If the parents stood by their decision to reassign the child as a girl, surgeons could remove the testicles and construct feminine external genitals immediately. When she was 11 or 12 years old, she could be given the female hormones.

Both twins traveled to Johns Hopkins at least once a year for the next 12 years for observation and study.

By the time of Imperato-McGinley et. al.'s initial report, Money was able to counter this threat to the learning theory by pointing to Joan's successful adoption of a female gender role, while her brother "John" was a typical little boy.[465] In an interview with *Rolling Stone* (the only journal – academic or otherwise – to give a full report of the John/Joan case) Dr. William Reiner, a child psychologist at Johns Hopkins, says:

> It was the hallmark case. It was the hallmark case because it was followed and written up a number of times by Money and then essentially was the source of his statements – and subsequent statements in any of the pediatric textbooks in endocrinology, urology, surgery and psychology – that you can reassign the sex of a child because it's the social situation that is the most important.[466]

Even after Money lost track of the twins, the John/Joan case was cited in the literature as support for the learning theory. In philosophical terms, it acted as a "crucial experiment." Scientists and researchers took Money's word for it that Joan's transition to a little girl was smooth and uncomplicated. Decades later, a team of researchers reported on another case of ablatio penis, beginning with a discussion of Money's guidelines for sex-reassignment:

Money, J., and Tucker, Patricia (1975). Sexual Signatures: On Being a Man or a Woman. Boston, Little and Brown.

[465] See, for instance, Money, J. (1972). Man & Woman, Boy & Girl: The Differentiation and Dimorphism of Gender Identity from Conception to Maturity. New York, New American Library.

[466] Colapinto, J. (1997). "The True Story of John/Joan." Rolling Stone Magazine **775**: 54 - 97.

> J. Money used these guidelines in a case of a biologically normal male infant (one of a pair of monozygotic twins) whose penis was accidentally ablated during a circumcision at the age of 7 months. The decision to reassign the infant boy to the female sex was made at 17 months, with surgical castration and initial genital reconstruction occurring at 21 months. Money reported follow-up data on this child through the age of 9 years. [John/Joan and family did not stop attending the Johns Hopkins clinic until the twins were over 12 years old. Conflicting dates and timelines are one of the factors bedeviling discussions of the John/Joan case.] Although the girl was described as having many "tomboyish" behavioral traits, a female gender identity had apparently differentiated. Thus, it was concluded that gender identity is sufficiently incompletely differentiated at birth as to permit successful assignment of a genetic male as a girl, in keeping with the experiences of rearing.[467]

The John/Joan case served not only as a counterexample to the findings of Imperato-McGinley et. al., it reinforced Money's initial recommendations concerning the treatment of individuals with ambiguous genitalia – until 1997.

Diamond, eager to follow up on the case, finally tracked down Joan. As it turns out, Joan's gender transition was far from smooth. In contrast to Money's glowing reports, Joan was a tomboy, refused to wear dresses or play with dolls, and repeatedly stated that she wanted to be a boy. As a final blow, Joan, at the age of fourteen, adopted a male gender identity and later underwent operations to remove breast tissue acquired

[467] Bradley, S., et. al. (1998). "Experiment of Nurture: Ablatio Penis at 2 Months, Sex Reassignment at 7 Months, and a Psychosexual Follow-up in Young Adulthood." Pediatrics **102**(1).

through estrogen treatment and a phalloplasty. Now a he, he eventually married.[468] The crucial experiment was a failure.

Proponents of the biological theory cite this development as an unambiguous triumph of nature over nurture. A year after Diamond's electrifying report, an editorial in a nursing journal claims:

> [T]he story [of John/Joan] reverses two beliefs widely held by clinicians: (a) that children are psychosexually neutral at birth and (b) that healthy psychosexual development depends upon the appearance of the genitals.[469]

In contrast to both scientific narratives – Money's and Diamond's – the reality was much more cloudy. It can be argued that Joan was not raised unambiguously as a girl, so the gender "switch" was not an either/or case. In addition, the family's history of mental illness (the father was an alcoholic, the mother a life-long depressive, and both twins eventually committed suicide) makes the twins less-than-ideal test subjects.[470] Finally, it is precipitous to base theories of psychosexual development on a single case – an observation which almost every article about the case from scientific journals *fails* to make.[471]

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[468] Diamond, M., and Sigmundson, Keith (1997). "Sex Reassignment at Birth: Long-term Review and Clinical Implications." Archives of Pediatrics and Adolescent Medicine **151**(3).

[469] Haller, K. (1998). "When John Became Joan." Journal of Obstetric, Gynecologic, and Neonatal Nursing **27**(1): 11.

[470] For more information, see Colapinto, J. (1997). "The True Story of John/Joan." Rolling Stone Magazine **775**: 54 - 97. Also, Colapinto, J. (2004). Gender Gap: What Were the Real Reasons Behind David Reimer's Suicide?, Slate. **2007**.

[471] In his review of endocrine influences on gender identity, Byne notes that there have been only four documented cases of *ablatio penis* with female gender reassignment before the age of two,

In spite of these complications, the John/Joan case is cited in reviews and textbooks as strong evidence that gender identity is innate and determined, at least in part, by prenatal hormones.[472] This hypothesis underlies theories about the etiology of transsexuality.

VII. Conclusion

While it is not immediately apparent why the organization/activation model should apply to transsexuality in the first place, this application makes sense in light of the history of the field, as well as prevailing cultural presuppositions about gender congruity.

The categorical confusions surrounding medical and endocrinological investigations of transsexuality (and other atypical phenomena) hindered much of the early research. The eventual resolution of these confusions, especially those concerning the etiology of gender identity, served to shed light on the relative contributions of internal versus external influences on sexual and gendered behavior.

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and detailed information is available for only two of these cases. Like many before him, Byne discusses the John/Joan case in detail "because of the inordinate impact it has had on the field." Byne, W. (2006). "Developmental Endocrine Influences on Gender Identity: Implications for Management of Disorders of Sex Development." The Mount Sinai Journal of Medicine **73**(7): 950-959.

[472] For example, in their chapter on sexual development disorders, Conte and Grumbach write that studies by Diamond and others "suggest that prenatal exposure to androgen and the presence of genes on the Y chromosome can influence gender identity in the individual with ambiguous genitalia." Conte, F., and Grumbach, Melvin (2007). Disorders of Sexual Determination and Differentiation. Greenspan's Basic and Clinical Endocrinology. D. Gardner, and Shoback, Dolores. New York, McGraw Hill.

The endocrinological research into the phenomenon of transsexuality illustrates both the unifying power of the organization/activation model as well as the strength of mechanistic-inspired research programs. The unifying power is exemplied by the apparently incongruous extention of the model from a crucial resolution about the etiology of homosexuality to an explanation of transsexuality. The notion of psycho-neural pseudohermaphroditism, so crucial to the solution of the "problem" of homosexuality, provided a hypothetical answer (and inspired a research program) to that of transsexuality.

The history of research into the etiology of transsexuality provides strong support for my main thesis: that the explanatory power of the organization/activation model lies in its ability to explain a host of developmental endpoints. Both classifications of transsexuality – as a version of homosexuality or as a distinct phenomenon – explain it as the result of atypical sexual brain development. As such, both appeal to a Kitcherian sense of unification in their attempt to explain the etiology of transsexualism.

But the unifying power of the model brings explanatory problems in its wake, problems brought to the fore by the phenomenon of transsexuality. Because both conceptions of transsexuality conceive it to be a form of psycho-neural pseudohermaphroditism, this *general* explanation fails to shed light on the specifics of two developmental endpoints.

Nonetheless, the specificity, or modularity, of femininity acts as a major factor in the explanatory power of the organization/activation model in terms of both the etiology of (male) homosexuality, (male-to-female) transsexuality and, consequently, (male and female) heteronormative behavior. If researchers can discover the mechanisms that lead

to these specific developmental endpoints, as opposed to the rather vague explanations for the mismatch of gendered elements, than the organization/activation model will be able to fulfill its initial explanatory promise.

Conclusion

The early promise of hormones – that they could explain development in a much more satisfactory manner than external or genetic factors – set the research agenda for the field. From an initial, heuristic definition, hormones came to be classified in a more sophisticated fashion, as members of a particular chemical class.

But this conceptual and scientific innovation raised explanatory problems, some considered more important than others. Those problems considered crucial were resolved in a crucial fashion. Unlike crucial experiments, crucial resolutions occur in advance of unambiguous empirical evidence, determine the disciplinary matrix for the field, and appeal explicitly to explanatory unification. As such, crucial resolutions, and the general explanatory models they inspire, constitute a logic of discovery. The crucial resolution of the freemartin problem provided an answer to the lesser problems of timing and media. On a more general level, the crucial resolution of the problem of homosexuality provided a model that could explain both typical and atypical development.

But the historical development of the field, especially the monumental adoption of the organization/activation model, cannot be explained entirely by the ideal of explanation by unification. As scientists pursued the research agenda set by the organization/activation model, its tremendous unificatory promise, initially perceived as

its greatest strength, threatened to become its greatest weakness. This weakness is especially apparent with etiological investigations into the phenomenon of transsexuality.

The goal of scientists within this field has been, and continues to be, to cash out the initial predictions of the model in terms of biochemical mechanisms. While the model fulfills the criteria for genuinely explanatory mechanistic models, mechanism *per se* cannot explain the phenomenon of crucial resolutions. That is, mechanistic explanation cannot account satisfactorily for the adoption of general explanatory models.

Crucial resolutions appeal to unificatory ideals, but set the eventual explanatory goal for a field as that of uncovering underlying mechanisms. As such, I suggest that what counts as an explanation in the field of behavioral endocrinology is not a case of the same phenomenon being explained in two different ways, one mechanistic and the other unificationist, but rather a single explanatory model that explains the phenomena in terms of a general, mechanistic schema.

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