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GENES ASSOCIATED WITH SUBJECTIVE WELL-BEING IN A RECENT GWAS ARE ASSOCIATED WITH DECREASED DEPRESSIVE SYMPTOMS: POSSIBLE BIOLOGICAL MECHANISMS

Mackenzie Jones

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Subjective well-being (SWB) is heritable and associated with physical and mental health. A recent genome-wide association study (GWAS) of 298,420 individuals identified 3 single nucleotide polymorphisms (SNPs) associated with SWB. The amygdala is a brain region critical for behavioral vigilance and assigning emotional significance to stimuli. Elevated amygdala response to threat has frequently been observed in stress-related disorders such as depression making it a promising intermediate phenotype through which genetic risk for SWB may emerge. Here, we examined whether polygenic scores (PS) for SWB are associated with threat-related amygdala function.

Genomic, neuroimaging, and self-report data were available for 480 participants who completed the ongoing Duke Neurogenetics Study. Threat-related amygdala reactivity was assayed using an emotional face-matching task while functional magnetic resonance imaging data were acquired. Depressive symptomatology was assessed with self-report. We tested whether PS for SWB are associated with depressive symptoms and threat-related amygdala function. Further, given recent evidence from our lab that the association between amygdala reactivity and psychopathology is moderated by time of day, we examined whether this time of day moderated the association between SWB PS and amygdala function.

We found that polygenic scores associated with increased SWB were associated with decreased depression (significant at 4 of 10 p-value thresholds). There was a significant SWB PS x time of day interaction (significant at 5 of 10 p-value thresholds), such that among participants scanned earlier in the day, lower PS for SWB were associated with heightened amygdala reactivity.

These findings compliment evidence from our laboratory that elevated amygdala reactivity in the morning is associated with stress-related psychopathology as well as prior observations that SWB is reduced among those with late chronotypes. Diurnal-related variation in amygdala function may mechanistically link common genetic variation to SWB and related psychopathology.