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Gene expression in the prefrontal cortex associated with impulsivity

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Impulsivity has been identified as an important endophenotype of several mental health disorders notably including addiction. In the prefrontal cortex, the dorsolateral (dlPFC) and orbitofrontal (OFC) regions in particular have been associated with both impulse control generally as well as changes during disease. This work aimed to identify differences in gene expression in the prefrontal cortex associated with natural variation in impulsivity. The dlPFC and OFC were isolated from 70 demographically similar individuals with a mood disorder diagnosis or psychiatrically normal controls but without a history of illicit substance abuse. A psychological autopsy was performed on all individuals with screening on the Behavioral and Emotional Impulsivity subscales of the SIDP-IV. Total RNA was isolated and next generation sequencing was performed using an Illumina NextSeq 500 with a 150 bp paired-end protocol. Data was processed using multiple bioinformatic pipelines, cuffdiff and DESeq2, and functional enrichment was performed with Ingenuity Pathway Analysis. Extensive differential gene expression associated with impulsivity was identified in the OFC (194 genes), but not the dlPFC (18 genes). These differences were not associated with post-mortem interval, tissue pH, RNA quality, or age at death. Among the differentially expressed genes identified in the OFC was an overrepresentation of those involved in nervous system development, cellular proliferation, and catecholamine signaling. These findings demonstrate differences in gene expression associated with impulsivity, occurring in the absence of specific pathology, specifically in the orbitofrontal cortex and suggest natural variability inherent in predisposing factors for addiction.