

Transcriptome Differences in the Aging Schizophrenia Brain

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We discovered that transcript variants arising from splicing between annotated exons and repetitive elements in the brain are located in genomic regions associated with schizophrenia. Further analysis revealed that the expression of these transcript variants in the brain is altered during aging. Based on these findings, we investigated whether age related transcriptional differences exist in the schizophrenia brain. Exon expression in six age groups was measured separately in control and schizophrenia DLPFC samples using RNA sequencing data from the Common Mind, UC Davis, Psychencode and hippocampus samples from the Stanley array collection. Microarray data generated in DLPFC samples from the NIMH postmortem brain bank was also examined. Our reanalysis discovered 5189 exon expression differences in the control DLPFC samples from the Common Mind Collection. The majority of the differences resulted from comparisons between age groups less than 60 to those over 60 years. In the Common Mind DLPFC schizophrenia samples we discovered comparable 4853 exon expression differences between age groups. However, the trajectory and magnitude of age associated expression changes in the schizophrenia brain during age differed from that of unaffected controls. Mainly we found more differential expression between age groups under 60 years of age and less differential expression between age groups over 75 and less than 60 years of age. In the four replication cohorts we reanalyzed, we found no differences between age groups in the control samples. However, there were age related differences between the same age groups in the schizophrenia samples in 3 out of the four replication cohorts. We conclude that age related transcriptional differences likely exist in the schizophrenia brain. Our analysis demonstrates that the effect of aging on the brain is complex and should not be treated as a linear correlation.