GENE EXPRESSION

The dynamics of the brain transcriptome revealed

The tight regulation of gene expression in space and time is key to understanding how the complexity and variation within and between organisms can arise from a relatively simple DNA blueprint. Until now, few studies had been able to characterize the temporal dynamics of gene transcription in the human brain with the depth reported in two recent papers published in *Nature*.

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Kang *et al*. generated and analysed the spatio-temporal changes in gene expression that take place in 16 different brain areas, from 57 post-mortem human brains ranging in age from 5.7 weeks post conception to 82 years. They extracted the RNA content from a total of 1,340 tissue samples and examined both differential gene expression and exon usage across brain regions and over time. Furthermore, they identified 29 modules of co-expressed genes with distinct spatio-temporal expression patterns, which suggests that they are involved in particular biological processes, and identified genes exhibiting sex-biased expression during development.

They found that over 80% of the genes examined are differentially regulated across brain regions (reflecting anatomical differences) and/or over time, and that the greatest regional differences in expression occur during prenatal development. With age, regional transcriptomes become more similar. Differential spatio-temporal exon usage was also observed in over 90% of the genes expressed in the brain, highlighting the importance of alternative splicing mechanisms and gene promoters in generating transcript diversity.

As the expression pattern of individual genes or groups of genes that are associated with neurodevelopment or disease matched those reported in previous studies, the authors were able to confidently use their data set to generate spatio-temporal expression trajectories of genes associated with particular developmental processes or diseases, such as schizophrenia or autism spectrum disorder. They were also able to identify genes with significantly correlated expression patterns. Such genes are likely to also have a role in these developmental processes or diseases.

In another study, Colantuoni *et al*. focused on the gene expression pattern of the prefrontal cortex over time. They also note significant changes in expression throughout development and identify a consistent architecture of transcription across subjects from different races, despite the large number of genetic polymorphisms among them. Their study highlights waves of gene expression changes that occur during fetal development and that are reversed in early postnatal life. As expected, the expression of genes that are associated with cell division decreases during fetal development, whereas that of genes associated with synapse formation and function increases during late fetal development and early infancy. Interestingly, the rate of gene expression changes remains relatively low until 50 years of age, when it rises again mirroring the changes in gene expression that are seen in early postnatal life. This characterization of the ageing brain transcriptome is likely to shed new light on the mechanisms underlying age-related cognitive changes and neurodegeneration.

Both data sets are freely available, and the authors encourage researchers to further explore them and make comparisons with other data sets obtained from individuals in diseased states or non-human primates, to further our understanding of brain function and evolution.

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ORIGINAL RESEARCH PAPERS Kang, H. J. *et al.* Spatio–temporal transcriptome of the human brain. *Nature* **478**, 483–489 (2011) | Colantuoni, C. *et al.* Temporal dynamics and genetic control of transcription in the human prefrontal cortex. *Nature* **478**, 519–524 (2011).