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Exploring the cellular and temporal specificity of neurological disorder genes in human brain development

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Advancements in single-cell technologies have revolutionized transcriptomic investigations across diverse brain regions, enriching our understanding of the human brain. However, the challenge persists in accurately delineating the cell-type specificity of neurological disorders considering the developmental variations. To bridge this gap, we investigated neurological disorder gene expression dynamics throughout development by incorporating a single-cell transcriptome dataset spanning multiple developmental stages. We constructed a comprehensive single-cell atlas comprising 393,060 cells and nuclei, encompassing various developmental stages. We revealed distinctive temporal expression patterns of neurological disorder risk genes, including autism, and highlighted the temporal regulation of gene expression across neuronal and non-neuronal cell types. Individual neuronal lineages that diverged across the developmental stage exhibited distinct temporal expression patterns of different disorder risk genes. Similarly, lineage-specific expression patterns were observed in non-neuronal cell types, revealing an association between neurological diseases and cellular maturity determined by molecular profiles. Moreover, our investigation into regulatory mechanisms governing early brain development revealed an enrichment pattern wherein traits related to neurological diseases are predominantly concentrated within fetal cell types. Our study aims to facilitate unbiased comparisons of cell type-neuronal disorder associations at specific time points and offer insights into the dynamic changes of risk genes during development to promote a deeper understanding of neurological diseases.