Early life experience drives somatic mosaicism of the mouse brain

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Different cells within an individual contain different DNA sequences, a phenomenon known as somatic mosaicism. Such genomic variation arises from a variety of sources, including de novo copy number variants, replication errors, and DNA transposons. Somatic mosaicism was recently identified as a feature of normal, healthy brains. It has been suggested that somatic mutations contribute to brain plasticity, but it is unclear whether neuronal DNA sequences can be altered in response to environmental experience. Here we investigated whether early life experience mediates copy number of Long Interspersed Nuclear Element-1 (LINE-1 or L1) retrotransposons in specific regions of the mouse brain. L1 retrotransposons mobilize in the genome and insert copies of themselves into new locations, where they may affect gene expression or cellular function. We studied differences in maternal care as a model of early life experience. Rodents exhibit natural variations in maternal behavior that influence the neurodevelopment and adult behavior of their offspring. We developed assays for droplet digital PCR, as well as targeted single-cell sequencing approaches, to address the hypothesis that differences in maternal care influence L1 mobilization in the brain. By manipulating maternal care, we established a direct association of L1 copy number with experience. Further, we identified a potential mechanism for their expression and mobilization. Taken together, our observations indicate that early life experience can drive somatic variation in the genome via L1 retrotransposons.