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L1 retrotransposons in cocaine addiction

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Cocaine addiction (CA) is an important public health problem, with 2.2 million people age 12 or older reporting that they have used cocaine in the past 30 days. With no currently approved pharmacotherapy, after several decades of attempts, our need to develop an effective treatment for CA is greater than ever. Despite evidence for the heritability of CA, identification of alleles with even a small effect has been difficult. Therefore, alternative approaches to identifying genetic variants associated with CA are needed. We examined the role of neuronal polymorphic and somatic long interspersed element-1 (LINE1 or L1) retrotransposons, a type of mobile DNA element, with the potential of disrupting genes, in the context of CA. DNA was isolated from postmortem NeuN+ medial frontal cortex neuronal nuclei from 25 cocaine addicted persons and 26 age, sex and ethnicity matched controls. L1 specific DNA was amplified using PCR, and L1 amplicons were subject to next generation sequencing. Bioinformatics was used to align sequencing data to the human reference genome to identify L1s in neuronally expressed genes and the frequency of individual L1 insertions in our sample set. Insertions specifically relevant to CA were identified, and both reference and novel L1 retrotransposons were found among the CA samples. Independent validations of the bioinformatics data are ongoing, with effect sizes as high as 2.5 having been already validated. Our preliminary observations suggest that L1s contribute to the etiology of CA, and that L1s may expand the nature of risk alleles associated with CA.