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Genes and cognitive deficits in adolescent-onset methamphetamine use disorder: Preliminary evidence from a cross-sectional study

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248/250 words

Background:

Methamphetamine is the second most used illicit substance globally. More alarming, methamphetamine use typically begins early. This is a major concern as adolescence is a period of heightened vulnerability to substance use disorders. Evidence suggests that the interplay between gene polymorphisms, expression, and cognitive deficits may be contributing factors.

Methods:

People with a current DSM-5 diagnosis of methamphetamine use disorder (last use within 7 days) and matched-controls were recruited (N=92). Participants completed a cognitive task battery assessing speed of processing, cognitive flexibility, working memory, and inhibitory control. Whole blood was collected to assess polymorphisms and mRNA expression of genes of interest.

Results:

People with methamphetamine use disorders displayed deficits in all cognitive domains (ps<0.05). Inhibitory control performance correlated with age of onset of methamphetamine use (r= 0.458, p<0.05). Preliminary chi-square analyses revealed that distribution of the Pro4Thr polymorphism of the vesicular monoamine transporter 1 gene SLC18A1 was significantly different between controls and people who use methamphetamine ($\chi 2=8.21;p=0.017$), with the minor allele conferring a risk for

Commented [JK1]: Revised because 15 years don't sound too young, and I've seen reports as young as 10 in Australia: https://www.thecourier.com.au/story/2380969/children-as-young-as-10-using-ice-in-ballarat/

Commented [JK2]: VMAT1 right not 2?

methamphetamine use disorder (OR= 2.82). Pro4Thr was also associated with an earlier age of onset of methamphetamine use (p=0.41).

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Conclusions:

Our preliminary results suggest that polymorphisms and change in expression of the versicular monoamine transporter 1, a key regulator of cytosolic and synaptic dopamine levels, may be a risk factor for developing methamphetamine use disorder when meth use occurs early in life. Future steps include replication in a larger cohort, and investigation of gene-cognition interactions to better understand adolescent susceptibility for methamphetamine use disorder.

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