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Relationship between plasma extracellular vesicle miRNAs and measures of neuropsychiatric function in methamphetamine use disorder

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Abstract

Introduction

The long-term health effects of methamphetamine including cognitive impairments, anxiety, and depression, which can persist during recovery and are associated with poor treatment outcomes. Thus, biosignatures based on objectively quantifiable blood biomarkers that relate to neuropsychiatric data could be used clinically to monitor recovery. We previously identified seven plasma extracellular vesicle (EV) miRNAs that are differentially expressed in humans with active methamphetamine disorder (MA-ACT) vs. controls (CTL). Here we related the expression of plasma EVs and their miRNAs to measures of neuropsychiatric function.

Methods

We measured the concentration of tetraspanin+ (CD9, CD63, CD81) and platelet EVs (CD41) in MA-ACT and CTL participants by vesicle flow cytometry. MiRNA expression in plasma EVs isolated by size exclusion chromatography were assayed by TaqMan arrays. Plasma EV concentrations and miRNA expression levels were related to measures of anxiety (GAD), depression (PHQ-9), and memory (PRMQ).

Results

CD41+ EVs correlated with depression scores in MA-ACT plasma, while TS+ EVs did not correlate with any of the neuropsychiatric measures. For the seven EV miRNAs with differential expression in MA-ACT, four correlated with clinical features of methamphetamine use disorder: miR-374b-5p and -628-3p correlated with anxiety and memory scores, respectively, while miR-301a-3p, -382-5p, and -628-3p correlated with

methamphetamine use characteristics (e.g., frequency of use and lifetime exposure). The predicted gene targets of these four miRNAs identified pathways related to synaptic plasticity, neurodegeneration, neuroinflammation, and dopamine neuron function, which are all factors of methamphetamine dependency.

Discussion

These studies demonstrate the potential utility of plasma EVs to serve as metrics for recovery by relating EVs and miRNA cargo to clinical features of methamphetamine use.