Title: Magnetoencephalographic Correlates of Reward Processing in Mood Disorders

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Abstract:

Background

Ketamine has been identified as a promising, rapid-acting antidepressant, but its neural mechanism of action is still poorly understood. Previous research has suggested that its impact on reward processing circuitry may play a role in its antidepressant effect, though there have been conflicting reports on how it impacts behavioral aspects of reward processing. In this study, participants with a mood disorder (MD) and healthy controls (HC) completed a modified version of the Monetary Incentive Delay Task (MID) during a magnetoencephalography (MEG) scan. A subsample of the MD group completed a second scan either during (MD-Ket) or one day following (MD-KDB) an intravenous subanesthetic ketamine infusion (0.5 mg/kg). In this preliminary analysis of the MD sample, behavioral data (accuracy and reaction time, RT) was examined. Based on previous literature, it was predicted that ketamine would alter reward-related processing of monetary gains and losses in MD participants.

Methods

Twenty-six participants (23 MD, 3 HC) completed the MID task. In addition, within the MD sample, 12 participants received ketamine (5 MD-Ket and 7 MD-KDB). MEG data was recorded using a CTF 275 MEG system. In each session, accuracy was calculated and compared at baseline and following ketamine for monetary gain and loss trials. Bias scores were calculated by subtracting RT for loss trials from gain trials to compare reward-related biases at baseline and following ketamine, to control for acute drug effects on RT.

Results

Within the MD sample, there was a significant increase in accuracy for gain trials from baseline (66.8%) to ketamine (75.9%) ($t=-2.6$, $p<0.05$) and no difference in the accuracy of loss trials from baseline (64.7%) to ketamine (69.7%). In addition, there was a significant increase in RT bias from baseline (-2.8) to ketamine (-14.6) ($t=2.4$, $p>0.05$), reflecting faster reaction times to gains versus losses following ketamine.

Discussion

These findings suggest that ketamine alters reward-related behavior in MDs by motivating individuals towards gains over losses. Planned analyses will examine the effects of gain and loss trials on gamma power (a proxy measure of excitation-inhibition balance) for both MD and HC participants, in addition to examining the effect of ketamine on gamma power and anhedonia in the context of reward-related processes.

Funding Source: Intramural Research Program at the National Institute of Mental Health, National Institutes of Health

Keywords: reward processing, magnetoencephalography, mood disorders, ketamine