Neurocognitive Effects of Intravenous Ketamine Treatment in Treatment Resistant Depression

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BACKGROUND

- Ketamine is an NMDA receptor antagonist associated with learning and memory
- Limited pre-clinical evidence suggests neurotoxicity
- There is disagreement over how ketamine treatment for treatment resistant depression (TRD) impacts cognitive function[1,2,3,4]
- We conducted a clinical trial to examine biomarkers of remission to ketamine for resistant unipolar or bipolar depression
- We administered 3 acute intravenous ketamine infusions at a sub-anesthetic dose of 0.5 mg/kg over 11 days

AIMS

- Investigate possible effects of intravenous ketamine on cognition using the Repeatable Battery for the Assessment of Neuropsychological Status Update®, (**RBANS-Update**) pre- and post-infusions
- Determine if there are any deleterious effects of intravenous ketamine on cognition
- The RBANS-Update is a brief, individually administered battery[5] to measure cognitive decline or improvement

METHODS

- At baseline and 24 hours after the last infusion, the RBANS-Update was administered
- RBANS-Update is a validated and reliable cognitive battery of 12 subtests focused on 5 indexes of cognition: immediate memory, visuospatial/constructional, language, attention, and delayed memory
- Subtest raw scores are converted to standardized index scores by same-age peer groups
- The RBANS-Update was administered by trained raters for standardization
- Regular checks were made to insure inter-rater reliability

RESULTS

- We report 27 subjects that completed the acute phase of infusions and RBANS-Update at the University of Michigan and satellite Michigan State University – Pine Rest sites
- Preliminary analysis shows, regardless of clinical outcome, there was a significant improvement in all five cognitive indexes and by percentile rank (***see Table below***)
- Overall (total scaled score), there was significant improvement from percentile rank by age group at baseline (M=49.67, SD=27.19) to 24 hours post infusion 3 (M=72.14, SD=30.48) conditions; t(26)=-4.898, p = .000

RBANS Means and Standard Deviations by Index (N = 27)

	Index Score		Percentile	
Index	Baseline M (SD)	Post M (SD)	Baseline M (SD)	Post M (SD)
Immediate Memory	99.96 (16.10)	120.92 (17.99)	50.64 (31.58)	80.65 (23.08)
Visuospatial/ Constructional	96.79 (16.50)	103.69 (17.84)	43.57 (33.22)	58.62 (34.22)
Language	96.04 (9.25)	101.35 (12.14)	40.11 (21.53)	53.39 (25.96)
Attention	101.82 (18.49)	107.65 (16.02)	53.20 (33.41)	64.39 (29.85)
Delayed Memory	98.21 (14.38)	109.00 (15.36)	49.67 (24.61)	70.25 (26.68)
Total Scaled Score	98.07 (14.72)	113.25 (26.68)	49.79 (27.19)	72.14 (30.48)

What about remitters?

- An ANOVA compared the effect of remission on percentile rank
- Remission was defined as a score of ≤ 9 on the Montgomery–Åsberg Depression Rating Scale MADRS
- There was no significant difference in remitter group at baseline testing on percentile rank; F(1, 25) = .228, p = .638

DISCUSSION

- These preliminary data provide evidence of cognitive improvement, not decline, following administration of 3 IV ketamine infusions for depression
- Cognitive improvement may be mediated by improvement in depression, however, even individuals not achieving remission demonstrated cognitive improvement
- Because there was no difference between participants that experienced remission and did not experience remission at baseline, baseline differences between groups cannot account for the overall improvement

CONCLUSIONS

- These data are clinically reassuring that low doses of ketamine do not cause neuro-cognitive deficits
- Preliminary results may provide a glimpse into how ketamine effects neurocognitive functioning
- Future analysis on the mediators of cognitive improvement in this group will be explored, (e.g. demographics, multiple mental health diagnoses, and comorbidities)
- We also plan to explore how depression improvement mediates improved cognition as well as how cognitive performance may be linked to suicidal ideation[1]

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