Supplementary Material.

Age affects temporal response, but not durability, to serial ketamine infusions for treatment refractory depression

Psychopharmacology

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S1.

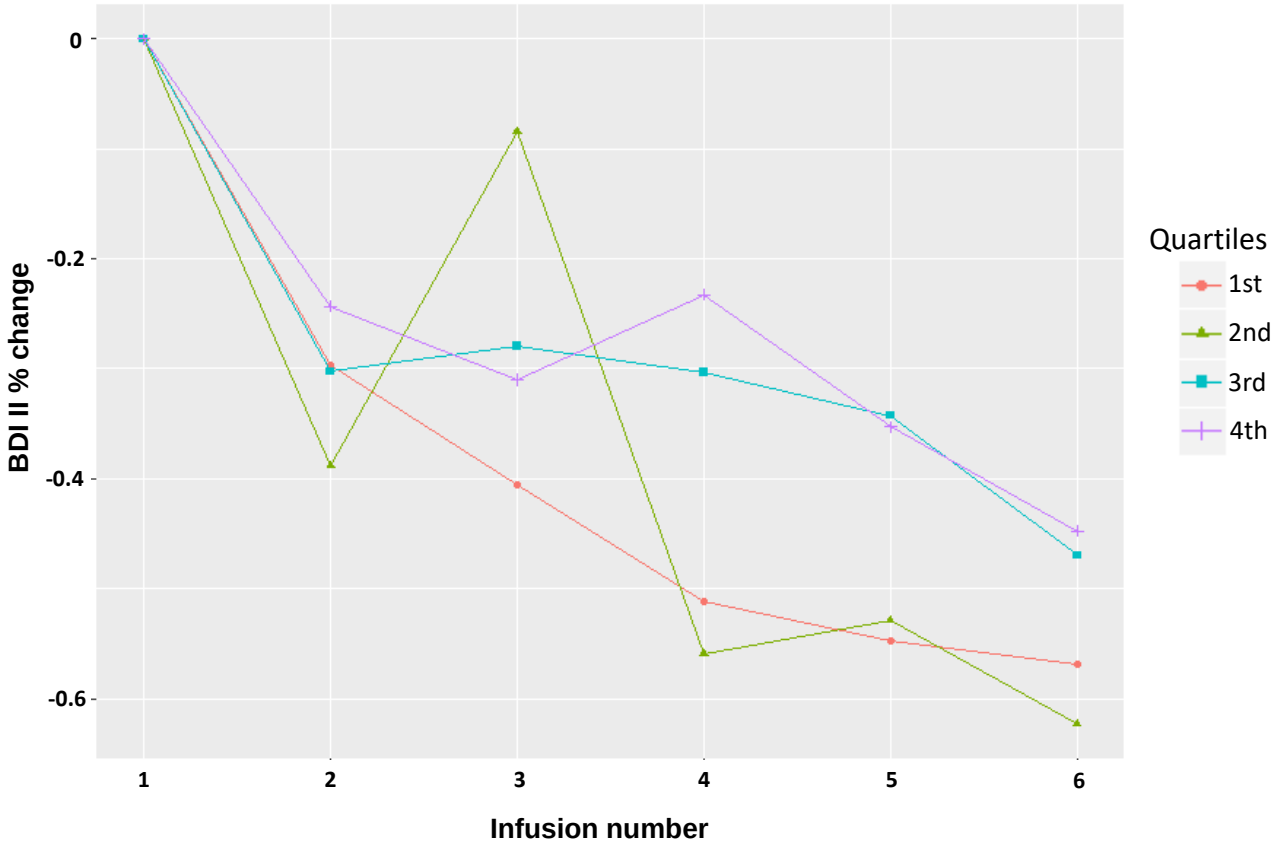

Fig. S1 Trajectories of response to serial ketamine infusions by age quartiles. BDI-II % change (decimated) over the six-infusion series grouped by age quartiles. Quartile ages (years): 1st = 24-41, 2nd = 41-54, 3rd = 54-65, 4th = 65-77).

Consideration of additional effects: *Sex, Body Mass Index, Ketamine Dose*

Sex: When the primary model was re-run with a sex covariate, a significant main effect of sex was observed (p=.009) and the Age X Time interaction remained significant (p=.030). Further, analysis on the male-only subsample revealed consistent effects, with follow-up contrasts in the male sub-sample still indicating significant age relationships between BDI-II percent change at time point 4 (p = 0.0057) and time point 5 (p = 0.03).

Body Mass Index (BMI): As patient BMI has been previously reported to correlate positively with clinical response to IV ketamine (Freeman et al. 2020; Niciu et al. 2014), we investigated this possible confound in our data in two ways 1. We ran a correlation of BMI versus age to investigate the extent to which age and BMI covaried in our sample. We found no significant correlation of BMI with age in our study population (Pearson's r = -.02, p=.979; spearman's rho = -.01, p=.929) and 2. We ran our linear-mixed model with BMI added as a factor. We found a positive relationship with percent change in BDI-II such that for each 1 unit increase in BMI there is a 1.4% increase in percent change in BDI-II (i.e., 1.4% less reduction in BDI-II). However, this did not change any of our previously reported effects regarding age or Age x Time effects.

Ketamine Dose: Seven patients had their ketamine dose adjusted during the infusion series (as described in the Methods Section), we re-ran the primary model investigating the Age X Time interaction with these seven patients excluded to confirm our reported effects were not confounded by differences in ketamine dose and found an almost identical pattern of statistical effects with the one difference being that the BDI-II percent change – age relationship at infusion #5 strengthened from a statistical trend in the whole sample to reach statistical significance in the sample restricted to patients that received 0.5mg/kg dosing.