

Evans et al: 7T ¹H-MRS in Major Depressive Disorder: a Ketamine Treatment Study

Supplementary Table 1: Summary of parameters for recent MRS studies of ketamine response

Study	Sequence	Field Strength	Metabolite	Size (cm)	rel to	Timepoints	Change from baseline/placebo	N	HV/MDD	[] ketamine
Milak (2015)	PRESS	3	Glx GABA	3.0x2.5x2.5	water	pre/during/immediately post infusion	y n	11	MDD	0.5mg/kg over 40 min
Rowland (2005)	PRESS	4	Glu Gln GABA	2.0x2.0x2.0	water	pre/during infusion	n y n	10	HV	0.27mg/kg over 10 min, then 0.00225 mg/kg per minute for ~2hrs
Stone (2012)	PRESS	3	Glu Glx GABA	2.0x2.0x2.0	water, csf normalized	pre/during infusion	y n n	13	HV	20 seconds of approx. 0.26mg/Kg followed by a slow infusion of approx. 0.42mg/Kg/Hr
Li (2017)	STEAM	7	Glu/Gln Glu Gln	2.0x1.5x1.0	water, csf normalized	pre/during infusion	y n n	12 ket, 14 pbo	HV	0.5mg/kg over 40 min or saline
Valentine (2011)	PRESS	4	Glu Gln GABA	3.0 x 1.5 x 3.0	Cr	pre,3hrs,48hrs/placebo	n,n,n n,n,n n,n,n	10	MDD	0.5mg/kg over 40 min or saline
Taylor (2012)	PRESS	3	Glu Glx Glx/Glu	3.0x2.0x2.0	Cr	pre,during,post	n n	8	HV	0.5mg/kg over 40 min
Salvadore (2012)	PRESS	3	Glx Glu Glx/Glu GABA	3.0x3.0x3.0	Cr	before	n/a	14	MDD	0.5mg/kg over 40 min

Supplementary Figure 1:

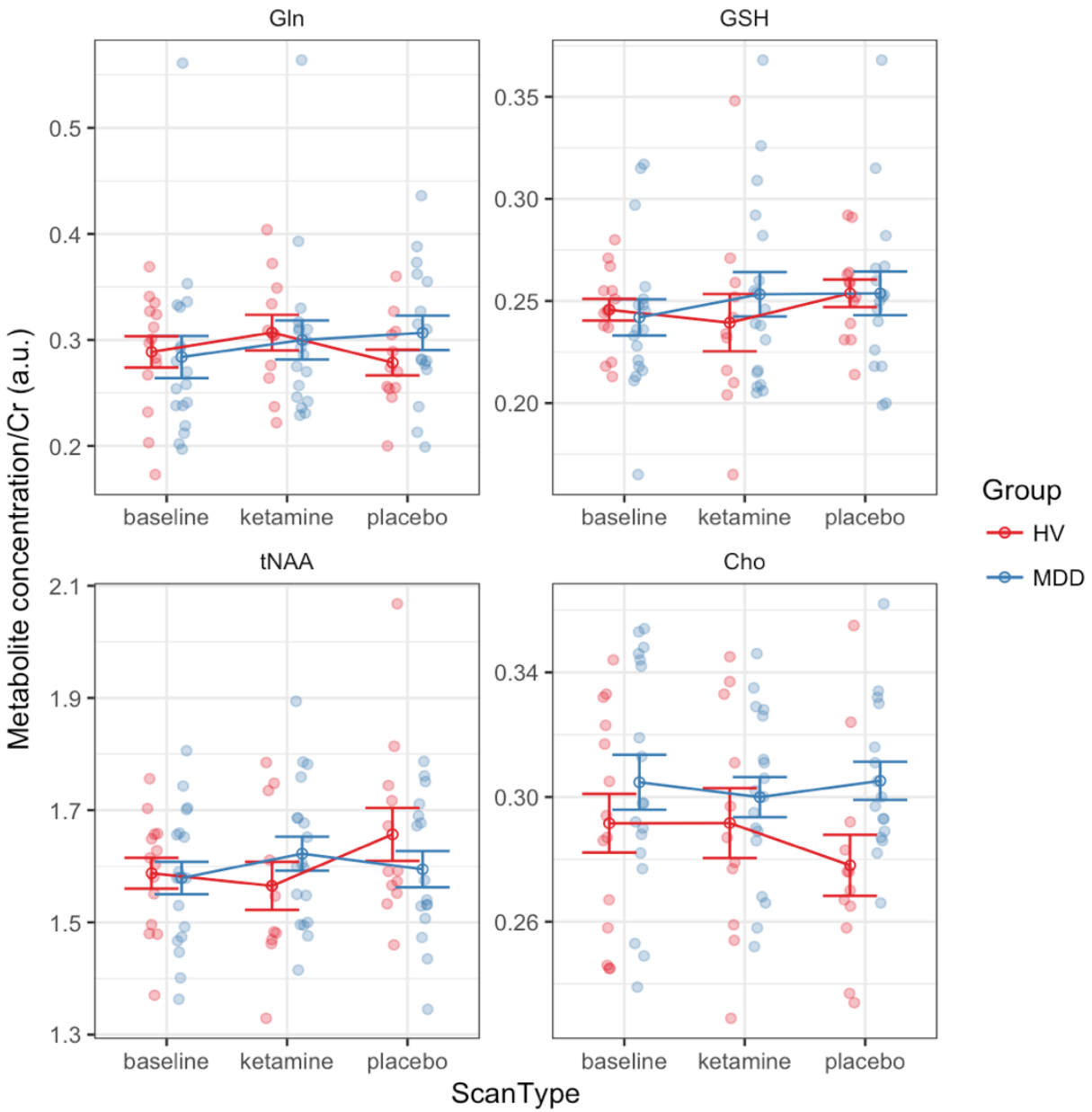


Figure S1. Group mean metabolite concentrations referenced to creatine for the healthy volunteers (HV, red) and major depressive disorder (MDD, blue) groups for each scan. Each filled circle represents the value for a subject. The open circle is the group mean, and the error

bars are the standard error.

Gln: Glutamine; GSH: Glutathione; Cho: Choline; tNAA: total N-Acetyl-Aspartate

Subgroup analysis

To further investigate the possibility of subgroups based on baseline glutamate, we conducted a brief post-hoc analysis and found that when our analyses were recalculated without the subgroup that had higher glutamate levels, a significant change ($\chi^2=4$, $p=0.046$) in glutamate levels between the post-ketamine and post-placebo scans was observed; however, this result should be interpreted with some caution due to its preliminary nature and the small number of subjects with high glutamate levels (four).

	Contrast	Value	χ^2	p-value
Glutamate	k-b	-0.16	14.43	0.0004
	k-p	0.08	3.97	0.05
	p-b	-0.09	5.68	0.03
Glutamine	k-b	-0.05	5.56	0.06
	k-p	0.01	0.18	0.67
	p-b	-0.04	5.25	0.06
Glutathione	k-b	-0.02	1.12	0.87
	k-p	0.01	0.96	0.87
	p-b	0.00	0.04	0.87
tNAA	k-b	-0.07	4.26	0.08
	k-p	0.08	6.83	0.03
	p-b	0.01	0.11	0.74
Choline	k-b	0.00	0.00	0.97
	k-p	-0.01	0.79	0.94
	p-b	-0.01	1.02	0.94