Data supplement for Prisciandaro et al., Effects of Gabapentin on Dorsal Anterior Cingulate Cortex GABA/Glutamate Levels and Their Associations With Abstinence in Alcohol Use Disorder: A Randomized Clinical Trial. Am J Psychiatry (doi: 10.1176/appi.ajp.2021.20121757)

TABLE S1. ¹H-MRS Quality Control Metrics by Treatment Group (Placebo vs. Gabapentin)

-	Placebo			Gabapentin			Total		
	n	Mean	(SD)	n	Mean	(SD)	n	Mean	(SD)
Glutamate F	it Error								
Scan 1	30	5.63	(0.49)	34	5.74	(0.57)	64	5.69	(0.53)
Scan 2	30	5.60	(0.56)	34	5.59	(0.50)	64	5.59	(0.53)
GABA Fit Err	ror								
Scan 1	31	5.85	(1.43)	37	6.71	(2.12)	68	6.32	(1.87)
Scan 2	31	5.67	(0.90)	37	6.17	(1.60)	68	5.94	(1.34)
FWHM									
Scan 1	31	8.74	(0.67)	37	9.03	(1.91)	68	8.90	(1.48)
Scan 2	31	9.08	(0.89)	37	8.89	(0.58)	68	8.98	(0.74)
Grey Matter	r								
Scan 1	31	0.51	(0.03)	37	0.50	(0.03)	68	0.50	(0.03)
Scan 2	31	0.51	(0.03)	37	0.50	(0.03)	68	0.51	(0.03)
White Matte	er								
Scan 1	31	0.26	(0.04)	37	0.27	(0.05)	68	0.26	(0.04)
Scan 2	31	0.26	(0.04)	37	0.27	(0.05)	68	0.27	(0.04)
CSF									
Scan 1	31	0.23	(0.05)	37	0.23	(0.06)	68	0.23	(0.05)
Scan 2	31	0.23	(0.04)	37	0.22	(0.06)	68	0.23	(0.05)
Water									
Scan 1	31	0.12	(0.03)	37	0.11	(0.03)	68	0.12	(0.03)
Scan 2	31	0.12	(0.02)	37	0.12	(0.03)	68	0.12	(0.02)
NAA SNR									
Scan 1	31	356.43	(66.53)	37	322.07	(97.45)	68	337.73	(85.92)
Scan 2	31	355.81	(68.34)	37	337.00	(85.31)	68	345.58	(78.05)

Note: Fit Error = standard deviation of the residual of the metabolite peak fit expressed as a percentage of the metabolite peak height; FWHM = Full Width Half Maximum of the unsuppressed water peak; Grey matter, white matter, and cerebrospinal fluid (CSF) = proportion of each quantity within the acquisition voxel; Water = integral of the unsuppressed water peak; NAA SNR = signal to noise ratio of the n-acetyl-aspartate peak. In addition to GABA Fit Error, FWHM and Water (unsuppressed water spectrum), as well as NAA SNR ("edit = OFF" condition spectrum), were each calculated from MEGA-PRESS data.

TABLE S2. ¹H-MRS Metabolite Levels by Treatment Group (Placebo vs. Gabapentin)

-	Placebo				Gabapentin			Total		
_	n	Mean	(SD)	n	Mean	(SD)	n	Mean	(SD)	
PRESS										
Glutamate										
Scan 1	30	11.03	(0.61)	34	11.07	(0.59)	64	11.05	(0.60)	
Scan 2	30	11.16	(0.74)	34	11.16	(0.78)	64	11.16	(0.75)	
Change	30	0.13	(0.83)	34	0.09	(0.78)	64	0.11	(0.80)	
Glx										
Scan 1	30	13.54	(0.93)	34	13.64	(0.84)	64	13.59	(0.88)	
Scan 2	30	13.88	(1.11)	34	13.97	(1.41)	64	13.93	(1.27)	
Change	30	0.35	(1.29)	34	0.32	(1.43)	64	0.33	(1.36)	
ml										
Scan 1	30	7.64	(0.86)	34	7.69	(0.95)	64	7.66	(0.90)	
Scan 2	30	7.71	(1.09)	34	7.89	(1.15)	64	7.81	(1.12)	
Change	30	0.07	(0.53)	34	0.21	(0.52)	64	0.14	(0.52)	
tCho										
Scan 1	30	2.31	(0.28)	34	2.25	(0.23)	64	2.28	(0.25)	
Scan 2	30	2.37	(0.26)	34	2.34	(0.27)	64	2.35	(0.26)	
Change	30	0.06	(0.22)	34	0.08	(0.13)	64	0.07	(0.18)	
tNAA										
Scan 1	30	10.62	(0.73)	34	10.70	(0.73)	64	10.66	(0.73)	
Scan 2	30	10.46	(0.83)	34	10.61	(0.96)	64	10.54	(0.90)	
Change	30	-0.15	(0.76)	34	-0.09	(0.76)	64	-0.12	(0.75)	
tCr										
Scan 1	30	7.87	(0.50)	34	7.77	(0.50)	64	7.82	(0.50)	
Scan 2	30	7.84	(0.47)	34	7.79	(0.50)	64	7.81	(0.48)	
Change	30	-0.03	(0.39)	34	0.02	(0.35)	64	0.00	(0.37)	
MEGA-PRES	S									
GABA										
Scan 1	31	1.02	(0.25)	36	0.99	(0.25)	67	1.01	(0.25)	
Scan 2	31	1.05	(0.21)	36	1.02	(0.21)	67	1.04	(0.21)	
Change	31	0.03	(0.26)	36	0.03	(0.28)	67	0.03	(0.27)	
Glx			·							
Scan 1	31	6.69	(1.22)	36	6.84	(1.02)	67	6.77	(1.11)	
Scan 2	31	6.67	(1.16)	36	6.79	(1.17)	67	6.73	(1.16)	
Change	31	-0.02	(0.96)	36	-0.05	(1.09)	67	-0.04	(1.02)	

Note: All metabolites were normalized to water, corrected for within-voxel cerebrospinal fluid fraction, and expressed in Institutional Units. Change was calculated as the value at Scan 1 (baseline) subtracted from the value at Scan 2. Glx = Glutamate + Glutamine, ml = Myo-inositol, tCho = Choline-containing Compounds, tNAA = N-Acetyl-containing Compounds, GABA = γ -Aminobutyric Acid.

TABLE S3. Percent Days Abstinent (PDA) Across Study by Treatment Group (Placebo vs. Gabapentin)

	Placebo				Gabapentin			Total		
Week	n	Mean	(SD)	n	Mean	(SD)	n	Mean	(SD)	
Between Scans	31	77.1%	(30.3%)	37	75.5%	(34.2%)	68	76.2%	(32.2%)	
4	30	69.5%	(32.3%)	37	62.6%	(41.2%)	67	65.7%	(37.3%)	
6	29	59.7%	(37.6%)	36	64.5%	(39.4%)	65	62.3%	(38.4%)	
8	28	55.4%	(39.4%)	33	63.9%	(42.2%)	61	60.0%	(40.8%)	
10	28	56.4%	(39.4%)	33	61.9%	(41.1%)	61	59.4%	(40.1%)	
12	27	52.9%	(40.6%)	33	62.1%	(42.6%)	60	58.0%	(41.6%)	
14	27	59.5%	(39.1%)	33	59.5%	(40.5%)	60	59.5%	(39.6%)	
16	27	64.0%	(37.4%)	33	56.4%	(40.2%)	60	59.8%	(38.8%)	

FIGURE S1. Glutamate/water Spaghetti Plots by Percent Days Abstinent Between Scans (Scan 1 = "pretreatment," Scan 2 = "posttreatment") by Treatment Group (Gabapentin vs. Placebo). Percent Days Abstinent Between Scans were binned according to the results of Johnson-Neyman analyses, described in *Results*. Solid black horizontal lines depict the average glutamate/water levels at each scan. Within each Percent Days Abstinent bin, the statistical significance of differences in pretreatment-to-posttreatment changes in glutamate/water levels between Treatment Groups is indicated. Glu = Glutamate, I.U. = Institutional Units. *p<0.05, ns. = not significant (i.e., p>0.05).

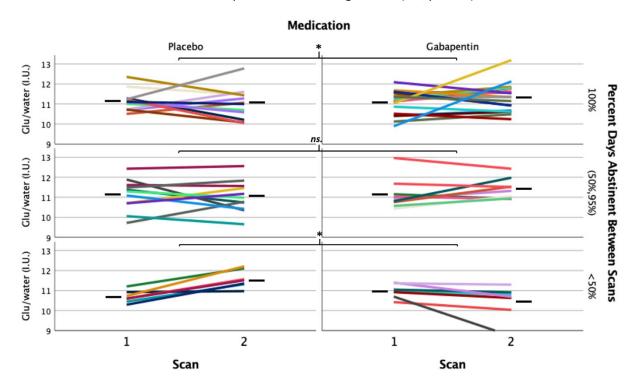


FIGURE S2. GABA/water spaghetti plots by Percent Days Abstinent Between Scans (Scan 1 = "pretreatment," Scan 2 = "posttreatment") by Treatment Group (Gabapentin vs. Placebo). Percent Days Abstinent Between Scans were binned according to the results of Johnson-Neyman analyses, described in *Results*. Solid black horizontal lines depict the average GABA/water levels at each scan. Within each Percent Days Abstinent bin, the statistical significance of differences in pretreatment-to-posttreatment changes in GABA/water levels between Treatment Groups is indicated. I.U. = Institutional Units. *p < 0.05, ns. = not significant (i.e., p > 0.05).

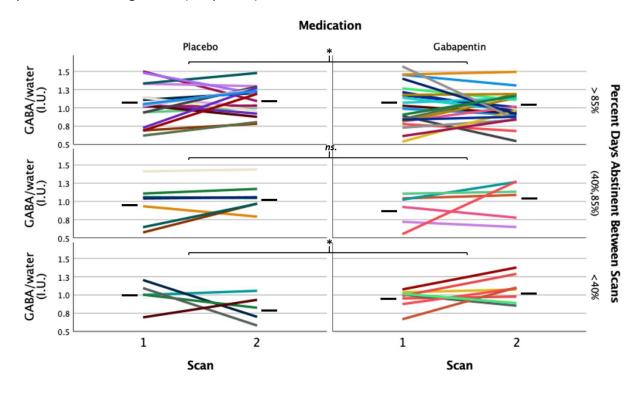


FIGURE S3. Percent days abstinent following scan 2 (i.e., early treatment; y-axis) by baseline dorsal anterior cingulate cortex (dACC) glutamate (n=64) levels (x-axis), normalized to water and expressed in Institutional Units (I.U.), by treatment group (red line = placebo, blue line = gabapentin). Error bands represent 95% confidence intervals.

