

Citations for the neurocognitive battery

Trails B (Reitan and Wolfson, 1985), Stroop Color Word Test (Golden, 1978), Auditory Verbal Learning Task (AVLT) (Rey, 1964), Wisconsin Card Sort Test (WCS) (Heaton et al., 1993), semantic (category) fluency (Spreen and Strauss, 1998), Controlled Oral Word Association (FAS) Test of phonemic fluency (Spreen and Benton, 1969), the Continuous Performance Task (CPT) identical pairs version (Cornblatt et al., 1988), letter number sequencing (Gold et al., 1997), N-back (Dobbs and Rule, 1989), Trails A (Reitan and Wolfson, 1985).

Other assessment citations

The Montgomery-Asberg Depression Rating Scale (MADRS) (Montgomery and Asberg, 1979). The Global Assessment of Functioning (GAF) (Hall, 1995). The Systematic Assessment For Treatment Emergent Events (Levine and Schooler, 1986).

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Supplemental Table 1 Baseline scores on cognition measures.

Domain	Study	Open-label	Double-blind	
	Treatment	Glycine (n=10)	Glycine (n=4)	Placebo (n=4)
	Measure	Mean (SD)	Mean (SD)	Mean (SD)
Processing speed	Trails A ^a	27.3 (12.6) ¹	37.3 (3.8) ⁴	38.5 (10.2)
	Stroop colors	64.9 (10.4) ¹	56.7 (8.6) ⁴	60.3 (17.9)
	Stroop words	90.1 (17.6) ¹	81.0 (6.1) ⁴	83.0 (22.4)
	Stroop color-word	41.7 (7.6) ¹	33.3 (4.2) ⁴	36.8 (11.0)
Verbal memory	AVLT immediate trials sum	51.0 (9.9) ³	46.8 (5.7)	38.8 (17.2)
	AVLT delay trial	9.6 (2.8) ³	10.0 (3.2)	9.3 (3.3)
	WCS perseverative errors ^a	8.2 (2.5) ^{3*}	13.0 (3.0) ⁴	6.8 (1.7) [*]
Executive functioning	WCS categories completed	3.0 (1.8) ³	1.7 (1.2) ⁴	3.8 (1.0) [*]
	Semantic fluency	36.8 (10.5) ¹	30.5 (8.9)	21.5 (7.9)
	Phonemic fluency	33.1 (12.6) ¹	31.5 (5.7)	35.3 (7.3)
	CPT-IP D-prime (2 digit)	3.3 (0.4) ²	2.9 (1.2) ⁴	3.1 (0.3)
	CPT-IP D-prime (3 digit)	3.0 (0.7) ²	1.9 (1.3) ⁴	1.9 (0.9)
Attention and Working Memory	CPT-IP D-prime (4 digit)	1.9 (0.8) ²	0.9 (0.4) ⁴	1.1 (0.4) ⁴
	CPT-IP reaction time (2 digit) ^a	433 (60) ²	462 (81) ⁴	424 (61)
	CPT-IP reaction time (3 digit) ^a	445 (41) ²	474 (81) ⁴	496 (83)
	CPT-IP reaction time (4 digit) ^a	457 (65) ²	471 (85) ⁴	512 (144) ⁴
	Letter number sequencing	14.4 (4.7) ¹	13.3 (3.3)	11.3 (4.6)
	1-back number correct	65.9 (18.0) ²	42.7 (19.4) ⁴	48.7 (12.4) ⁴
	2-back number correct	53.1 (23.4) ²	21.7 (12.3) ⁴	43.5 (24.7) ⁵
	Trails B ^a	69.9 (37.8) ¹	72.0 (13.5) ⁴	106.8 (52.6)

^a higher scores indicate greater impairment

n=10 for open label glycine and 4 for double blind glycine and for placebo, unless noted

¹ n=9, ² n=7, ³ n=8, ⁴ n=3, ⁵ n=2

* p<0.05 vs double blind glycine.

Supplemental Table 2 Mean (and SD) endpoint change and effect sizes for neuropsychological functioning measures¹.

Domain	Study Treatment Measure	Open-label Glycine (n=5)		Glycine (n=3)		Double-blind Placebo (n=2)		Between Groups ES
		Change Mean (SD)	Within Group ES	Change Mean (SD)	Within Group ES	Change Mean (SD)	Within Group ES	
		Processing speed	Trails A	-1 (2)	-0.26	-6 (11) ²	-0.61	
	Stroop colors ^a	-8.2 (8.5) [*]	-0.96	-6.5 (7.8) ²	-0.84	-3.5 (0.7)	-4.95	-0.47
	Stroop words ^a	-4.0 (6.6)	-0.60	-6.0 (8.5) ²	-0.71	3.5 (7.8)	0.45	-1.15
	Stroop color-word ^a	-2.6 (6.3)	-0.41	-7.5 (2.1) ²	-3.54	-5.0 (1.4)	-3.54	-1.31
Verbal memory	AVLT immediate trials sum ^a	-5.4 (7.1)	-0.76	-7.0 (7.2)	-0.97	-5.5 (2.1)	-2.59	-0.25
	AVLT delay trial ^a	-2.0 (2.3)	-0.85	-1.7 (1.2)	-1.44	-1.5 (0.7)	-2.12	-0.16
	WCS perseverative errors	-2.2 (1.7) ^{1*}	-1.32	7.5 (3.5) ²	2.12	4.0 (2.8)	1.41	1.09
Executive functioning	WCS categories completed ^a	-0.5 (0.6) ¹	-0.87	-2.0 (0.0) ^{2†}	<-10	0.0 (1.4)	0.00	-2.00
	Semantic fluency ^a	-0.8 (2.6)	-0.31	-11.0 (7.2)	-1.53	-1.5 (0.7)	-2.12	-1.61
	Phonemic fluency ^a	-5.4 (8.8)	-0.61	-1.7 (6.7)	-0.25	-2.5 (10.6)	-0.24	0.10
	CPT-IP D-prime (2 digit) ^a	-0.5 (0.5) ¹	-0.90	-0.3 (0.1) ²	-4.60	-1.0 ^{3†}		12.4 [†]
	CPT-IP D-prime (3 digit) ^a	-0.1 (0.1) ¹	-0.50	-0.7 (0.0) ^{2*}	-16.3	0.4 ^{3†}		-26.6 [†]
	CPT-IP D-prime (4 digit) ^a	0.2 (0.5) ¹	0.40	-0.7 (0.3) ²	-2.29	0.2 ^{3†}		-2.90 [†]
	CPT-IP reaction time (2 digit)	5 (30) ¹	0.17	-32 (74) ²	-0.44	57 ^{3†}		-1.21 [†]
Attention and Working Memory	CPT-IP reaction time (3 digit)	-7 (55) ¹	-0.12	-24 (76) ²	-0.31	11 ^{3†}		-0.46 [†]
	CPT-IP reaction time (4 digit)	52 (74) ¹	0.70	3 (44) ²	0.07	-58 ^{3†}		1.39 [†]
	Letter number sequencing ^a	-1.0 (2.0)	-0.50	0.0 (2.0)	0.00	-2.5 (0.7)	-3.54	1.49
	1-back number correct ^a	4.8 (16.3) ¹	0.29	-1.7 (6.7) ²	-0.25	-1 ^{3†}		-0.49 [†]
	2-back number correct ^a	8.0 (31.0) ¹	0.26	-5.5 (9.2) ²	-0.60	6 ^{3†}		-2.04 [†]
	Trails B	-8 (12)	-0.66	4 (16) ²	0.28	-28 (29)	-0.95	1.50

Patients were tested at baseline and at 8 weeks in the open-label study and at 12 weeks in the placebo-controlled study.

ES -- effect size. Negative change scores and ESs indicates improvement; negative between groups ES greater improvement with glycine than placebo. ^a sign reversed so that improvement appears as negative

n=5 for open label glycine, n=3 for double blind glycine, and n=2 for placebo, unless noted

¹ n=4, ² n=2, ³ n=1. * p<0.05 or † not calculable, paired or Student's t-test as appropriate. Within group ES not calculable when n=1.

Supplemental Table 3 Mean (and SD) baseline vital signs and weight.

Study Treatment	Open-label	Double-blind	
	Glycine (n=10) ¹	Glycine (n=4)	Placebo (n=4)
Measure	<u>Mean (SD)</u>	<u>Mean (SD)</u>	<u>Mean (SD)</u>
Systolic BP	119 (20)	115 (6)	115 (16)
Diastolic BP	71 (10)	63 (3)	62 (7)
Pulse	68 (9)	83 (18)	67 (12)
Weight, kg	81.4 (38.5)	53.6 (5.2)	58.1 (13.8)

All comparisons n.s.

1 n=9 for weight

Supplemental Table 4 Mean (and SD) baseline laboratory values.

Study Treatment	Open-label	Double-blind	
	Glycine (n=9)	Glycine (n=2)	Placebo (n=1)
Measure	Mean (SD)	Mean (SD)	Mean (SD)
WBC	6.5 (1.9)	10.2 (0.1)	5.0
Hemoglobin	14.3 (1.4)	15.0 (0.9)	16.7
Glucose	93.1 (20.8) ¹	95.5 (20.5)	88.0
BUN	14.9 (5.6) ¹	10.5 (2.1)	11.0
Creatinine	0.89 (0.16) ¹	1.00 (0.14)	1.20
Sodium	140 (1) ¹	142 (3)	142
Potassium	4.4 (0.5) ¹	4.7 (0.1)	5.0
Chloride	104 (2) ¹	104 (2)	101
Bicarbonate	25.6 (2.7) ¹	24.5 (2.1)	31.0
Calcium	9.3 (0.7)	9.8 (0.4)	9.5
AST	20 (14) ¹	16 (4)	19
ALT	24 (11) ¹	16 (5)	16
GGT	20 (9) ¹		
Bilirubin	0.5 (0.1) ¹	1.4 (1.1)	0.9
Albumin	4.6 (0.3) ¹	5.2 (0.1)	5.4
Cholesterol	161 (21) ¹		
Triglycerides	95 (41) ¹		

¹ n=8. Blank cells indicate laboratory test not acquired.

Supplemental Table 5 Effect sizes and mean (and SD) endpoint change in laboratory values.

Study Treatment	Open-label		Double-blind			Between Groups ES
	Glycine (n=9)	Within Group ES	Glycine (n=2)	Within Group ES	Placebo (n=1)	
Measure	Change Mean (SD)		Change Mean (SD)		Change	
WBC	0.2 (2.0)	0.08	-3.1 (0.1)*	-31.1	-0.2	-28.5
Hemoglobin	-0.3 (0.8)	-0.40	0.9 (1.0)	0.91	1.7	-0.81
Glucose	-5.0 (20.4) ¹	-0.25	-1.0 (21.2)	-0.05	2.0	-0.14
BUN	1.6 (7.4) ¹	0.22	-1.0 (2.8)	-0.35	6.0	-2.47
Creatinine	0.05 (0.11) ¹	0.47	-0.05 (0.07)	-0.71	0.00	-0.71
Sodium	0 (2) ¹	0.21	-2 (1)	-2.12	-1	-0.70
Potassium	-0.2 (0.4) ¹	-0.67	-0.4 (0.2)	-2.67	0.4	-5.56
Chloride	0 (3) ¹	-0.08	-1 (0)	-3.07	-1	0.00
Bicarbonate	-1.6(3.8) ¹	-0.43	0.0 (1.4)	0.00	-3.0	2.13
Calcium	0.1 (0.5)	0.22	0.3 (0.8)	0.35	0.9	-0.71
AST	-3 (9) ¹	-0.31	-1 (1)	-0.71	1	-1.42
ALT	-7 (10) ¹	-0.67	-4 (1)	-6.36	7	-16.2
GGT	-2 (3) ¹	-0.76				
Bilirubin	0.0 (0.1) ¹	0.00	-0.2 (0.3)	-0.71	0.1	-1.07
Albumin	0.0 (0.1) ¹	-0.27	0.1 (0.1)	0.71	0.2	-0.71
Cholesterol	-8 (23) ¹	-0.37				
Triglycerides	4 (55) ¹	0.07				

* p<0.05, paired t-test. Within paired and Student's t's not calculable when n=1.

¹ n=8. Blank cells indicate laboratory test not acquired.

Within group ES, paired t-test, and Student's t-test not calculable when n=1.