

TABLE S1. Risk of bias domains and steps taken to avoid bias

Domain	Steps taken to minimize bias
Selection bias, random sequence generation	Participants were randomized to treatment arm by an independent pharmacy using an appropriate random sequence generation; the study team and participants were not aware of randomization condition and remained blind to it for the duration of the study
Selection bias, allocation concealment	Allocation was conducted by an independent pharmacy; the study team and participants were not aware of allocation and remained blind to it for the duration of the study.
Performance bias, blinding of participants and personnel	Medication and placebo were of identical appearance and neither study participants nor study personnel were aware of the nature of the treatment (i.e. double-blind design). Active and placebo treatments were administered using identical procedures.
Blinding of outcome assessment	Outcome assessors were blinded to treatment condition. Analysis at the end of the study was conducted by an independent statistical company separate to the study team using pre-specified approaches. The statistical analysis plan was agreed in advance of database lock and in advance of unblinding.
Attrition bias, incomplete outcome data	Attrition was extremely similar across treatment arms. All available outcome data were analyzed.
Reporting bias, selective reporting	Instruments and outcome measures were finalized prior to database lock and analysis.
Other bias	This study did not involve any industry funding.

TABLE S2. Adjusted means, standard error, and 95% CI for the adjusted means

		Placebo				Memantine			
		Mean	SE	95% CI		Mean	SE	95% CI	
				Lower	Upper			Lower	Upper
NIMH	Baseline	12.21	0.54	11.14	13.28	12.67	0.49	11.70	13.64
	Week 2	10.58	0.56	9.48	11.67	7.55	0.54	6.50	8.61
	Week 4	10.76	0.57	9.64	11.89	7.11	0.54	6.04	8.17
	Week 6	11.08	0.59	9.92	12.24	6.08	0.54	5.01	7.15
	Week 8	11.10	0.58	9.95	12.24	5.62	0.53	4.57	6.67
SDS total	Baseline	9.37	0.97	7.46	11.27	10.38	0.89	8.63	12.13
	Week 2	7.22	1.00	5.26	9.18	6.83	0.97	4.91	8.74
	Week 4	8.54	1.03	6.52	10.57	4.35	0.99	2.41	6.29
	Week 6	8.65	1.07	6.54	10.75	3.24	1.00	1.28	5.20
	Week 8	7.88	1.03	5.85	9.90	4.32	0.97	2.42	6.22
HAM-A	Baseline	5.11	0.65	3.83	6.38	7.10	0.60	5.93	8.27
	Week 2	3.74	0.66	2.44	5.03	4.24	0.64	2.98	5.50
	Week 4	3.74	0.68	2.40	5.08	3.62	0.65	2.34	4.90
	Week 6	3.51	0.70	2.14	4.89	3.87	0.65	2.59	5.15
	Week 8	3.85	0.69	2.49	5.20	3.35	0.64	2.09	4.60
MGH total score	Baseline	19.47	0.70	18.09	20.84	19.30	0.64	18.05	20.55
	Week 2	17.29	0.72	15.87	18.70	14.46	0.70	13.08	15.84
	Week 4	17.28	0.75	15.82	18.75	12.11	0.72	10.70	13.52
	Week 6	16.68	0.78	15.14	18.22	11.65	0.74	10.20	13.10
	Week 8	16.41	0.76	14.92	17.90	12.37	0.72	10.95	13.78