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Supplementary Material

Article Title: Glutamatergic Agents as Add-On Medication for the Treatment of Obsessive-Compulsive Disorder: A Systematic Review and Meta-Analysis

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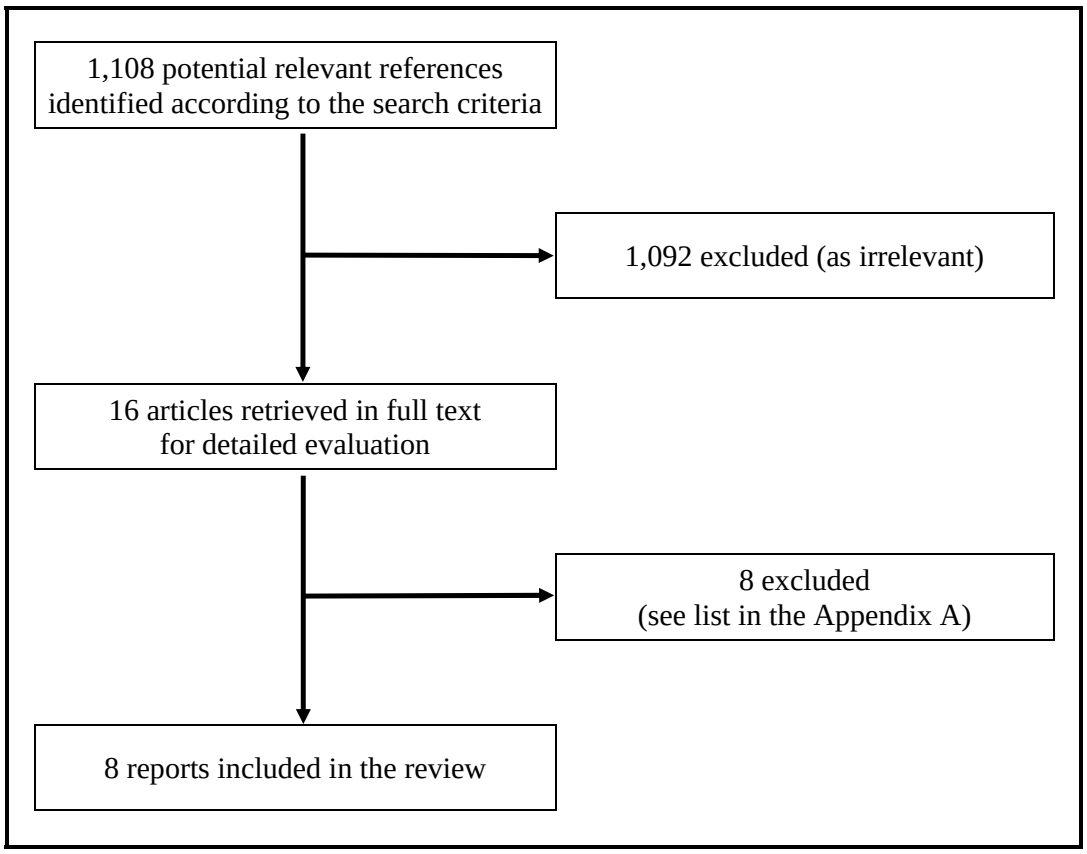
This Supplementary Material has been provided by the author(s) as an enhancement to the published article. It has been approved by peer review; however, it has undergone neither editing nor formatting by in-house editorial staff. The material is presented in the manner supplied by the author.

eAppendix 1.
I. Rejected studies

Article	Reason for rejection
Bloch MH, Wasylink S, Landeros-Weisenberger A, Panza KE, Billingslea E, Leckman JF, Krystal JH, Bhagwagar Z, Sanacora G, Pittenger C. Effects of ketamine in treatment-refractory obsessive-compulsive disorder. Biol Psychiatry. 2012 Dec 1;72(11):964-70.	No RCT.
Hussain A, Dar MA, Wani RA, Shah MS, Jan MM, Malik YA, Chandel RK, Margoob MA. Role of lamotrigine augmentation in treatment-resistant obsessive compulsive disorder: a retrospective case review from South Asia. Indian J Psychol Med. 2015 Apr-Jun;37(2):154-8	No RCT.
Koran LM, Aboujaoude E, Bullock KD, Franz B, Gamel N, Elliott M. Double-blind treatment with oral morphine in treatment-resistant obsessive-compulsive disorder. J Clin Psychiatry. 2005 Mar;66(3):353-9.	Monotherapy.
Kumar TC, Khanna S. Lamotrigine augmentation of serotonin re-uptake inhibitors in obsessive-compulsive disorder. Aust N Z J Psychiatry. 2000 Jun;34(3):527-8.	No RCT.
Lafleur DL, Pittenger C, Kelmendi B, Gardner T, Wasylink S, Malison RT, Sanacora G, Krystal JH, Coric V. N-acetylcysteine augmentation in serotonin reuptake inhibitor refractory obsessive-compulsive disorder. Psychopharmacology (Berl). 2006 Jan;184(2):254-6	No RCT.
Pasquini M, Biondi M. Memantine augmentation for refractory obsessive-compulsive disorder. Prog Neuropsychopharmacol Biol Psychiatry. 2006 Aug 30;30(6):1173-5	No RCT.
Poyurovsky M, Weizman R, Weizman A, Koran L.Memantine for treatment-resistant OCD. Am J Psychiatry. 2005 Nov;162(11):2191-2.	No RCT.
Rodriguez CI, Kegeles LS, Levinson A, Feng T, Marcus SM, Vermes D, Flood P, Simpson HB. Randomized controlled crossover trial of ketamine in obsessive-compulsive disorder: proof-of-concept. Neuropsychopharmacology. 2013 Nov;38(12):2475-83	Monotherapy.

II. Flow diagram of the study



eAppendix 2. Assessment of bias

We used the Cochrane Collaboration's tool for assessing the risk of bias. These criteria may be considered sufficiently strict. This included extracting of six domains and judging them. The consensual authors' judgment were either "Yes", indicating low risk of bias, "No" indicating high risk of bias, or "Unclear" indicating unknown risk of bias. The criteria to assess the studies were:

Domain	Description	Review Author's Judgement
Sequence generation	Describe the method used to generate the allocation sequence	Was the allocation sequence adequately generated? (Yes, No, Unclear)
Allocation concealment	Describe the method used to conceal the allocation sequence	Was allocation adequately concealed? (Yes, No, Unclear)
Blinding of participants, personnel, and outcome	Describe all measures used to blind participants and personnel	Was knowledge of the allocated intervention adequately prevented during the study? (Yes, No, Unclear)
Incomplete outcome data	Describe the completeness of outcome data for each main outcome including attrition and exclusions from the analysis.	Were incomplete outcome data adequately addressed? (Yes, No, Unclear)
Selective outcome reporting	State how the possibility of selective outcome reporting was examined by the review authors and what was found.	Are reports of the study free of suggestion of selective outcome reporting? (Yes, No, Unclear)
Other sources of bias	State any important concerns about bias not addressed in the other domains.	Was the study apparently free of other problems that could put it at high risk of bias?

Greenberg et al., 2009

Domain	Description	Review Author's Judgement
Sequence generation	Randomized trial. Block design.	**Yes.**
Allocation concealment	Assignment envelopes are not described. Drug containers of identical appearance.	**Unclear.**
Blinding of participants, personnel, and outcome	Double blind trial.	**Yes.**
Incomplete outcome data	Available data analysis.	**Yes.**
Selective outcome reporting	All prespecified outcomes of interest are reported in the pre-specified way.	**Yes.**
Other sources of bias	High attrition rates and small sample size.	**No.**

Mowla et al., 2010

Domain	Description	Review Author's Judgement
Sequence generation	Standard randomization procedure generated by computer.	**Yes.**
Allocation concealment	Assignment envelopes not described. Tablets of same color and shape.	**Unclear.**
Blinding of participants, personnel, and outcome	Double blind trial.	**Yes.**
Incomplete outcome data	Completers' analysis.	**No.**
Selective outcome reporting	All prespecified outcomes of interest are reported in the pre-specified way.	**Yes.**
Other sources of bias	The study appears to be free of other sources of bias.	**Yes.**

Berlin et al., 2011

Domain	Description	Review Author's Judgement
Sequence generation	Randomized trial, use of permuted blocks.	**Yes.**
Allocation concealment	Assignment envelopes not described. Identical tablets and drug containers.	**Unclear.**
Blinding of participants, personnel, and outcome	Double blind trial.	**Yes.**
Incomplete outcome data	Intention-to-treat analysis.	**Yes.**
Selective outcome reporting	All prespecified outcomes of interest are reported only in graphs.	**No.**
Other sources of bias	The study appears to be free of other sources of bias.	**Yes.**

Afshar et al., 2012

Domain	Description	Review Author's Judgement
Sequence generation	Randomized trial. Random-list generator software.	**Yes.**
Allocation concealment	Assignment envelopes and drug containers are not described.	**Unclear.**
Blinding of participants, personnel, and outcome	Double blind trial.	**Yes.**
Incomplete outcome data	The analysis is described as ITT, however it is actually an available case analysis.	**Yes.**
Selective outcome reporting	Rates of partial response are not reported.	**No.**
Other sources of bias	The study appears to be free of other sources of bias.	**Yes.**

Bruno et al., 2012

Domain	Description	Review Author's Judgement
Sequence generation	Randomized trial. Randomized codes generated by computer.	**Yes.**
Allocation concealment	Assignment envelopes are not described. Identical appearing capsules.	**Unclear.**
Blinding of participants, personnel, and outcome	Double blind trial.	**Yes.**
Incomplete outcome data	Intention-to-treat analysis.	**Yes.**
Selective outcome reporting	All prespecified outcomes of interest are reported in the pre-specified way.	**Yes.**
Other sources of bias	The study appears to be free of other sources of bias.	**Yes.**

Ghaleiha et al., 2013

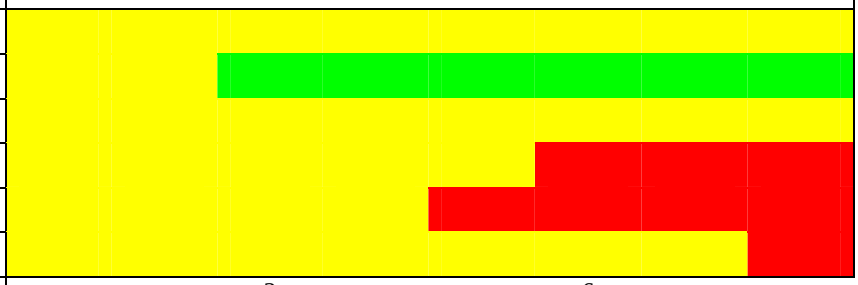
Domain	Description	Review Author's Judgement
Sequence generation	Computerized random number generator.	**Yes.**
Allocation concealment	Opaque and sealed assignment envelopes. Placebo with the same taste and shape.	**Yes.**
Blinding of participants, personnel, and outcome	Double blind trial.	**Yes.**
Incomplete outcome data	The analysis is described as ITT, however it is actually an available case analysis.	**Yes.**
Selective outcome reporting	Unclear report of response rates. Endpoint scores in YBOCS are not reported.	**No.**
Other sources of bias	The study appears to be free of other sources of bias.	**Yes.**

Haghighi et al., 2013

Domain	Description	Review Author's Judgement
Sequence generation	Randomized trial. Computerized random number generator.	**Yes.**
Allocation concealment	Patients drew raffle tickets from a ballot box. Tablets and drug containers of identical appearance.	**Yes.**
Blinding of participants, personnel, and outcome	Double blind trial.	**Yes.**
Incomplete outcome data	Completers' analysis.	**No.**
Selective outcome reporting	All prespecified outcomes of interest are reported in the pre-specified way.	**Yes.**
Other sources of bias	The study appears to be free of other sources of bias.	**Yes.**

Afshar et al., 2014

Domain	Description	Review Author's Judgement
Sequence generation	Randomized trial. Random number generator software.	**Yes.**
Allocation concealment	Assignment envelopes are not described. Identical appearing tablets.	**Unclear.**
Blinding of participants, personnel, and outcome	Double blind study.	**Yes.**
Incomplete outcome data	Completers' analysis	**No.**
Selective outcome reporting	All prespecified outcomes of interest are reported in the pre-specified way.	**Yes.**
Other sources of bias	The study appears to be free of other sources of bias.	**Yes.**

Domain	Assessment
Sequence generation	
Allocation concealment	
Blinding	
Missing Data	
Selective Reporting	
Other Bias	
	3 6

Yes	Unclear	No

Risk of bias graph. The semaphore colors provide a visual impression of the quality of the study reports for meta-analysis; green: condition is fulfilled; yellow: condition is questionable, and red: condition is not fulfilled and risk of bias is present. The allover risk for bias is low.

eAppendix 3. Egger's test