

## Supplementary material: Endophenotypes of executive functions in Obsessive Compulsive Disorder? A meta-analysis in unaffected relatives

**Table S1.** Table presenting the studies included in the meta-analysis and the executive measures employed on each study

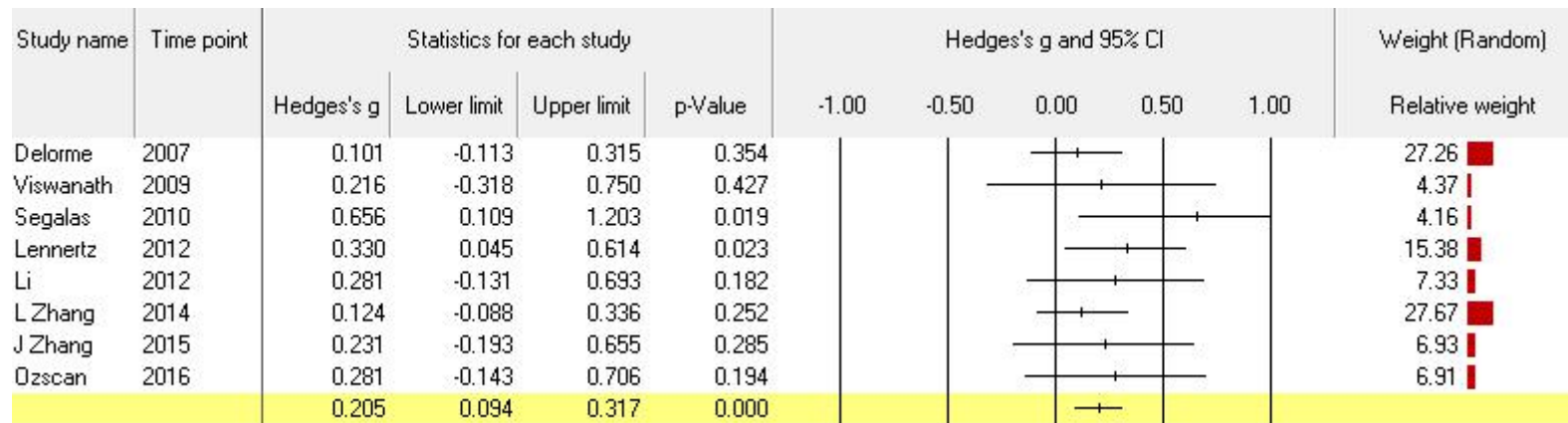
First author and year of publication	Title, tasks included in the analysis and number of participants	Main findings	Country of the study site
Riesel et al. (2011)	<p><b>Title:</b> Overactive error-related brain activity as a candidate endophenotype for obsessive-compulsive disorder: evidence from unaffected first-degree relatives.</p> <p><b>Tasks:</b> Flanker task</p> <p><b>N of participants:</b> 30 unaffected relatives; 30 healthy controls</p>	Both unaffected relatives and OCD patients showed increased error-related brain potentials.	Germany
Rajender et al. (2011)	<p><b>Title:</b> Study of neurocognitive endophenotypes in drug-naïve obsessive-compulsive disorder patients, their first-degree relatives and healthy controls.</p> <p><b>Tasks:</b> Tower of London (TOL), Wisconsin Card Sorting Test (WCST), Stroop task, Digit Vigilance Test (DVT)</p> <p><b>N of participants:</b> 30 unaffected relatives; 30 healthy controls</p>	Both patients with OCD and their FDRs were found to have significantly impaired delayed verbal recall, set-shifting ability, response inhibition and visuo-constructive abilities as compare with healthy controls.	India
Lennertz et al. (2012)	<p><b>Title:</b> Antisaccade performance in patients with obsessive-compulsive disorder and unaffected relatives: further evidence for impaired response inhibition as a candidate endophenotype.</p> <p><b>Tasks:</b> Tower of London (ToL), Trail Making Test (TMT), Visual Organisation Test (VOT), Auditory Verbal Learning test (AVLT), Verbal Fluency test, Visual working memory test</p> <p><b>N of participants:</b> 30 unaffected relatives; 30 healthy controls</p>	The OCD patients and the unaffected relatives showed increased antisaccade error rates compared with the healthy control group. Only OCD patients but not the relatives were impaired with regard to visuospatial functions, problem-solving, and processing speed.	Germany
Carrasco et al. (2013)	<p><b>Title:</b> Increased error-related brain activity in youth with obsessive-compulsive disorder and unaffected siblings.</p> <p><b>Tasks:</b> Flanker task</p> <p><b>N of participants:</b> 19 unaffected relatives, 40 healthy controls</p>	Compared to healthy controls, error related negativity amplitude was significantly increased in both pediatric OCD patients and their unaffected siblings.	USA
Lochner et al. (2016)	<p><b>Title:</b> Altered cognitive response to serotonin challenge as a candidate endophenotype for obsessive-compulsive disorder.</p> <p><b>Tasks:</b> Cambridge Gambling task (CGT)</p> <p><b>N of participants:</b> 13 unaffected relatives, 27 healthy controls</p>	There was a significant interaction between serotonergic challenge and group for risk adjustment on the Cambridge Gamble Task. Change in risk adjustment was similar in OCD patients and relatives and differed significantly from controls.	South Africa
Chamberlain	<p><b>Title:</b> Impaired cognitive flexibility and motor inhibition in unaffected</p>	Unaffected first-degree relatives and OCD patient	UK

et al. (2007)	<p>first-degree relatives of patients with obsessive-compulsive disorder.</p> <p><b>Tasks:</b> Intradimensional/Extradimensional Shift task, Stop signal task, Cambridge Gambling task (CGT)</p> <p><b>N of participants:</b> 20 unaffected relatives; 20 healthy controls</p>	<p>probands showed cognitive inflexibility and motor impulsivity compared to controls. Decision making was intact.</p>	
Cavedini et al. (2010)	<p><b>Title:</b> Executive dysfunctions in obsessive-compulsive patients and unaffected relatives: searching for a new intermediate phenotype.</p> <p><b>Tasks:</b> Iowa Gambling Task (IGT), Tower of Hanoi (ToH), Wisconsin Card Sorting Test (WCST)</p> <p><b>N of participants:</b> 35 unaffected relatives; 31 healthy controls</p>	<p>OCD patients showed impairments in decision making, planning, and mental flexibility. Their relatives performed poorer at these tests than healthy controls.</p>	Italy
Li et al. (2012)	<p><b>Title:</b> Neuropsychological study of patients with obsessive-compulsive disorder and their parents in China: searching for potential endophenotypes.</p> <p><b>Tasks:</b> Tower of Hanoi (ToH), Wisconsin Card Sorting Test (WCST), Trail Making Test (TMT), Verbal Fluency test, Wechsler Memory Scale (WMS) Visual Memory subtest</p> <p><b>N of participants:</b> 48 unaffected relatives, 87 healthy controls</p>	<p>Both OCD patients and their parents showed impairments problem-solving ability compared to healthy subjects.</p>	China
Zhang L. et al. (2015)	<p><b>Title:</b> Dissociation of decision making under ambiguity and decision making under risk: a neurocognitive endophenotype candidate for obsessive-compulsive disorder.</p> <p><b>Tasks:</b> Stroop task, Wisconsin Card Sorting Test (WCST), Digit Span, Iowa Gambling Task (IGT), Game Of Dice task (GDT), Trail Making Test (TMT), Tower of London (ToL), Verbal fluency test</p> <p><b>N of participants:</b> 55 unaffected relatives, 55 healthy controls</p>	<p>OCD patients and the relatives performed worse than the healthy controls on the Iowa Gambling Task but were unimpaired on the Game of Dice Task. The results indicate that decision making under ambiguity differs from decision making under risk.</p>	China
Zhang J. et al. (2015)	<p><b>Title:</b> Neuropsychological dysfunction in adults with early-onset obsessive-compulsive disorder: the search for a cognitive endophenotype.</p> <p><b>Tasks:</b> Wisconsin Card Sorting Test (WCST), Stroop task, Tower of Hanoi (ToH), Digit Span, Trail Making Test (TMT)</p> <p><b>N of participants:</b> 40 unaffected relatives, 40 healthy controls</p>	<p>OCD patients performed significantly worse than healthy controls on the Tower of Hanoi, and the Stroop and Wisconsin tests, indicating impairments in planning, mental flexibility and inhibitory control. The performance of their relatives on the Stroop and Wisconsin tests also differed from that of healthy controls.</p>	China
Vaghi et al.(2017)	<p><b>Title:</b> Hypoactivation and Dysconnectivity of a Frontostriatal Circuit During Goal-Directed Planning as an Endophenotype for Obsessive-Compulsive Disorder.</p> <p><b>Tasks:</b> One touch spatial planning task</p>	<p>OCD patients and their relatives manifested hypoactivation of the right dorsolateral prefrontal cortex during goal-directed planning coupled with reduced functional connectivity between this</p>	UK

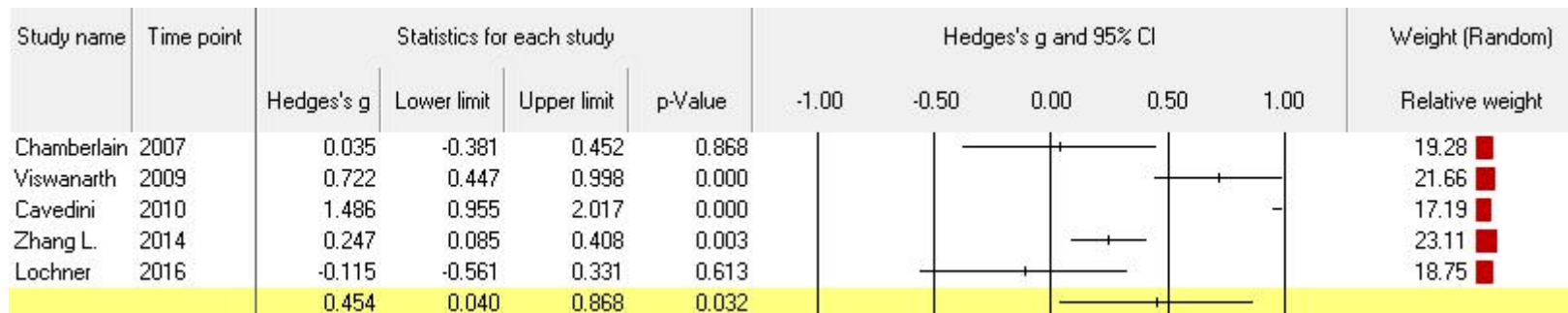
	<b>N of participants:</b> 19 unaffected relatives, 20 healthy controls	cortical region and the basal ganglia.	
Ozscan et al. (2016)	<b>Title:</b> Neuropsychological, electrophysiological and neurological impairments in patients with obsessive compulsive disorder, their healthy siblings and healthy controls: Identifying potential endophenotype(s). <b>Tasks:</b> Trail Making Test (TMT), Wisconsin Card Sorting Test (WCST), Digit Span, Stroop task, Controlled Word Association Test (CWAT), Category Fluency test (CFT), Figural memory test (FMT) <b>N of participants:</b> 18 unaffected relatives, 21 healthy controls	Executive functions and visuospatial integration were highly impaired in patients and slightly in their siblings compared to controls.	Turkey
De Wit et al. (2012)	<b>Title:</b> Presupplementary motor area hyperactivity during response inhibition: a candidate endophenotype of obsessive-compulsive disorder. <b>Tasks:</b> Stop signal task <b>N of participants:</b> 17 unaffected relatives, 37 healthy controls	Patients with OCD had greater stop-signal reaction times relative to healthy comparison subjects. The numerical stop-signal reaction time difference between unaffected relatives of the patients and comparison subjects failed to reach significance.	Netherlands
Van Velzen et al. (2015)	<b>Title:</b> Altered inhibition-related frontolimbic connectivity in obsessive-compulsive disorder. <b>Tasks:</b> Stop signal task <b>N of participants:</b> 17 unaffected relatives, 37 healthy controls	OCD patients, and to a lesser extent also their unaffected relatives, showed altered connectivity between the inferior frontal gyrus and the amygdala during response inhibition.	Netherlands
Bey et al. (2018)	<b>Title:</b> Impaired planning in patients with obsessive-compulsive disorder and unaffected first-degree relatives: Evidence for a cognitive endophenotype. <b>Tasks:</b> Tower of London (ToL) <b>N of participants:</b> 76 unaffected relatives, 102 healthy controls	Both OCD patients and their unaffected relative showed deficient TOL performance across a range of task conditions compared to healthy subjects, indicating deficits in problem solving.	Germany
Menzies et al. (2007)	<b>Title:</b> Neurocognitive endophenotypes of obsessive-compulsive disorder. <b>Tasks:</b> Stop signal task <b>N of participants:</b> 31 unaffected relatives, 31 healthy controls	Both OCD patients and relatives had delayed response inhibition on the Stop-Signal task compared with healthy controls.	UK
Riesel et al. (2019)	<b>Title:</b> Error-related brain activity as a transdiagnostic endophenotype for obsessive-compulsive disorder, anxiety and substance use disorder. <b>Tasks:</b> Flanker task <b>N of participants:</b> 50 unaffected relatives, 130 healthy controls	Increased event related negativity amplitudes were found in OCD patients and their unaffected relatives compared to healthy subjects.	Germany
Tezscan et al. (2018)	<b>Title:</b> Situation Awareness in Obsessive Compulsive Disorder and Their Relatives: an Endophenotype Study. <b>Tasks:</b> Situational Awareness test (SAtest) <b>N of participants:</b> 50 unaffected relatives, 41 healthy controls	OCD patients and their relatives performed significantly worse than the control group in the situation awareness task. There were no significant differences between OCD patients and their relatives.	Turkey

Segalas et al. (2010)	<p><b>Title:</b> Memory and strategic processing in first-degree relatives of obsessive compulsive patients.</p> <p><b>Tasks:</b> Digit Span</p> <p><b>N of participants:</b> 25 unaffected relatives, 25 healthy controls</p>	Unaffected relatives of OCD patients and healthy controls did not show differences on most measures of verbal memory. However, during the recall and processing of non-verbal information, deficits were found in the OCD patients and their relatives compared to healthy controls.	Catalonia
Viswanath et al. (2009)	<p><b>Title:</b> Cognitive endophenotypes in OCD: a study of unaffected siblings of probands with familial OCD.</p> <p><b>Tasks:</b> Iowa Gambling Task (IGT), Wisconsin Card Sorting Test (WCST), Tower of London (ToL), Trail Making Test (TMT), Controlled Oral Word Association Test (COWA), Stroop task, Delayed Alternation Test (DAT)</p> <p><b>N of participants:</b> 25 unaffected relatives, 25 healthy controls</p>	Unaffected relatives showed significant deficits in tests of decision making and behavioural reversal i.e., the Iowa Gambling Task (IGT) and the Delayed Alternation Test (DAT) respectively, but performed adequately in other tests.	India
Delorme et al. (2007)	<p><b>Title:</b> Shared executive dysfunctions in unaffected relatives of patients with autism and obsessive-compulsive disorder.</p> <p><b>Tasks:</b> Tower of London (ToL), Trail Making Test (TMT), Verbal Fluency Task, Association Fluency Task, Design Fluency Task</p> <p><b>N of participants:</b> 64 unaffected relatives, 47 healthy controls</p>	In the Tower of London test, unaffected relatives showed significantly lower scores and longer response times compared to controls. No differences were observed between OCD relatives and healthy controls in the four other tasks (verbal fluency, design fluency, trail making test and association fluency).	France

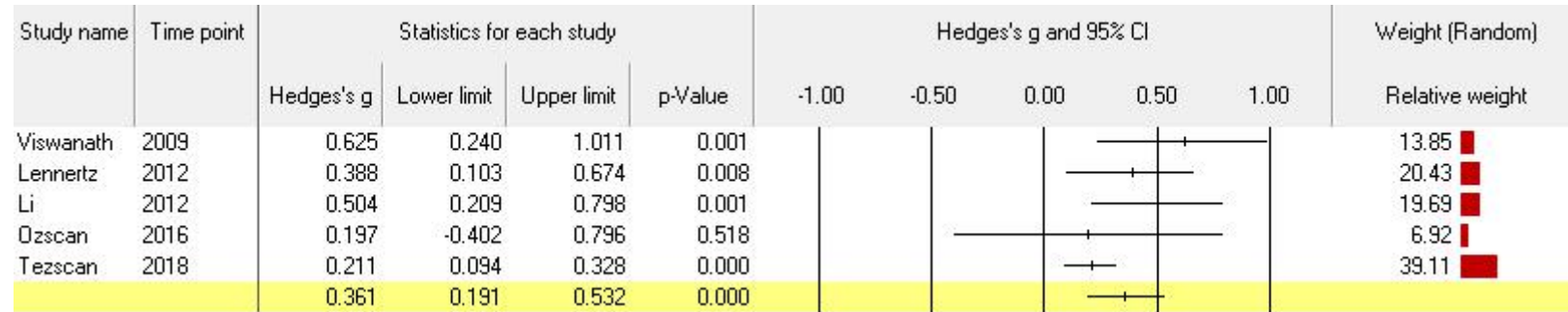
**Figure S1.** Forest plot of the meta-analysis of the studies comparing unaffected relatives of patients with Obsessive-compulsive disorder and unrelated healthy controls for the domain of verbal fluency



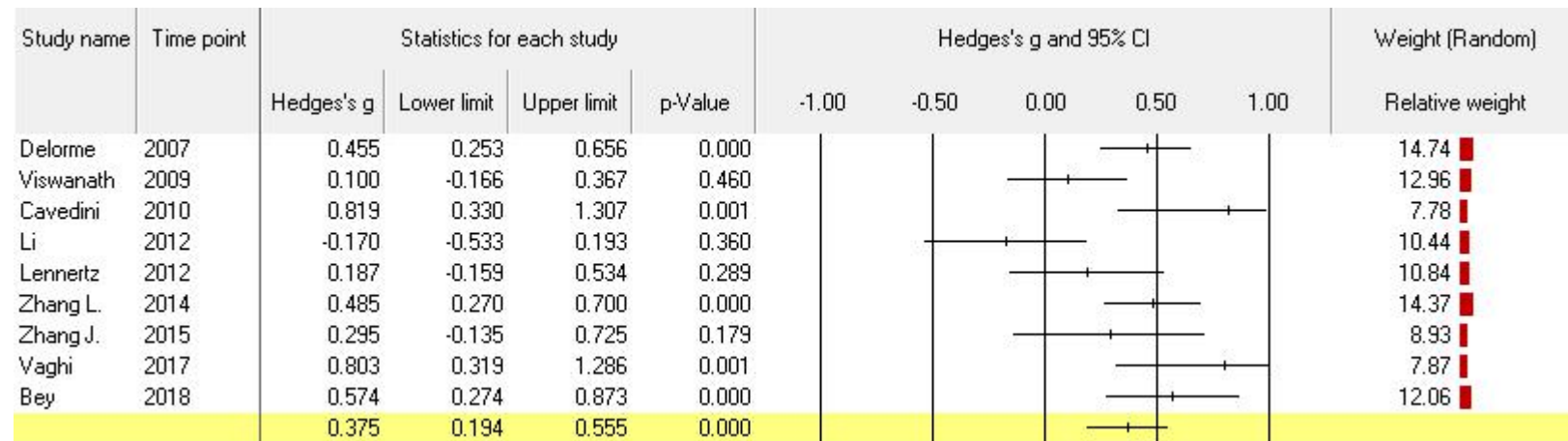
**Figure S2.** Forest plot of the meta-analysis of the studies comparing unaffected relatives of patients with Obsessive-compulsive disorder and unrelated healthy controls for the domain of decision making



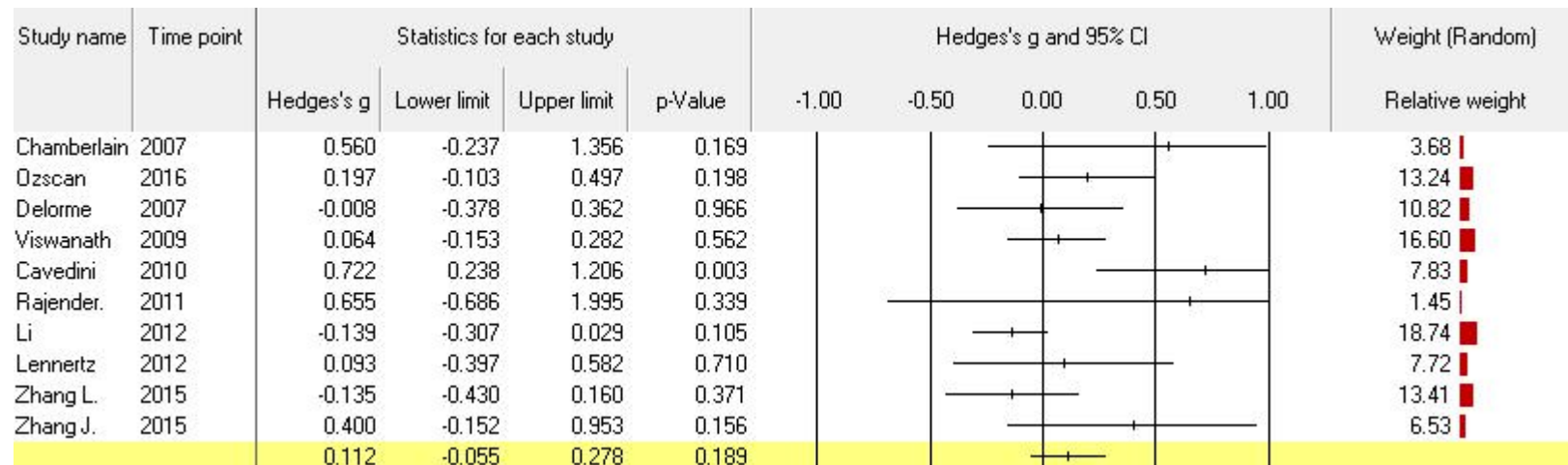
**Figure S3.** Forest plot of the meta-analysis of the studies comparing unaffected relatives of patients with Obsessive-compulsive disorder and unrelated healthy controls for the domain of visuospatial working memory



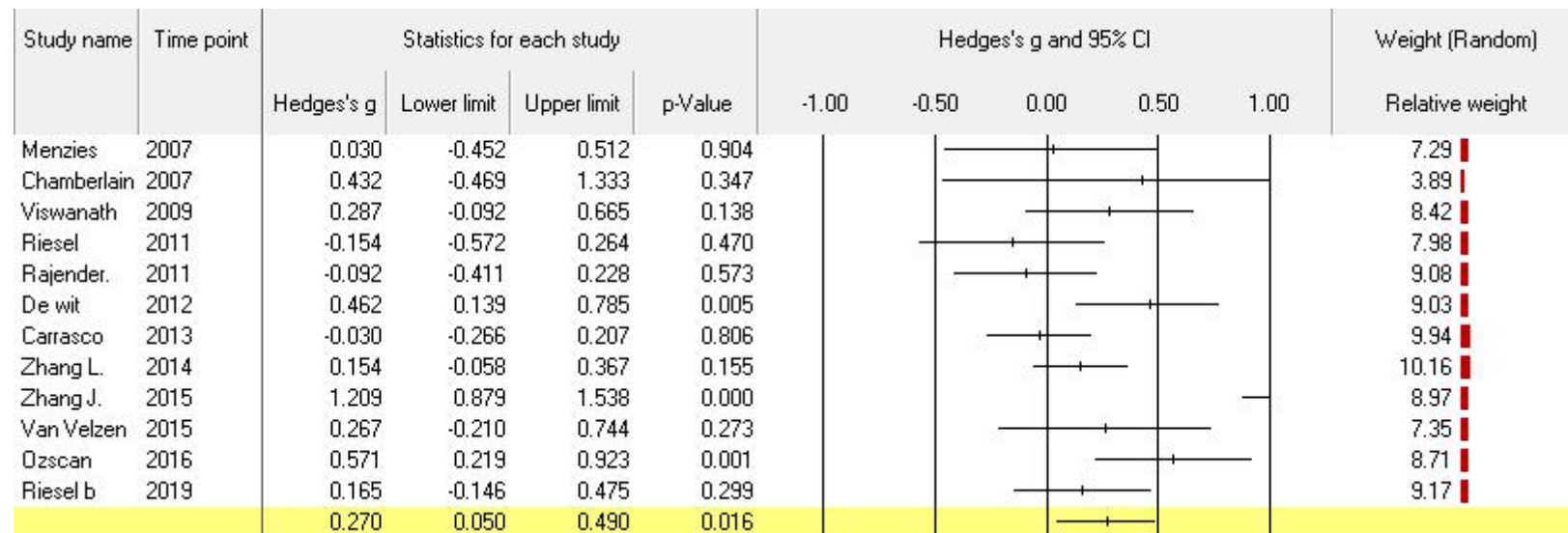
**Figure S4.** Forest plot of the meta-analysis of the studies comparing unaffected relatives of patients with Obsessive-compulsive disorder and unrelated healthy controls for the domain of planning



**Figure S5.** Forest plot of the meta-analysis of the studies comparing unaffected relatives of patients with Obsessive-compulsive disorder and unrelated healthy controls for the domain of set shifting



**Figure S6.** Forest plot of the meta-analysis of the studies comparing unaffected relatives of patients with Obsessive-compulsive disorder and unrelated healthy controls for the domain of inhibition/selective attention



**Figure S7.** Funnel Plot indicating no publication bias.

