


ORIGINAL ARTICLE

Meta-analyses of clinical neuropsychological tests of executive dysfunction and impulsivity in alcohol use disorder

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ABSTRACT

Background: Promising models for cognitive rehabilitation in alcohol treatment rest on a more nuanced understanding of the associated impairments in the multifaceted domains of executive functioning (EF) and impulsivity. **Objectives:** This meta-analysis examined the effects of alcohol on the individual subcomponents of EF and impulsivity in recently detoxified participants, including 1) Inhibition & Self-Regulation, 2) Flexibility & Set Shifting, 3) Planning & Problem Solving, 4) Reasoning & Abstraction, and 5) Verbal Fluency. Impulsivity was further examined through an analysis of motor, cognitive, and decisional subcategories. **Method:** Investigators searched, coded, and calculated effect sizes of impairments demonstrated in a broad range of neuropsychological tests for EF. A total of 77 studies were selected covering 48 years of research with a sample size of 5140. **Results:** Findings ranged from a Hedges' *g* effect size of 0.803 for Inhibition to a Hedges' *g* of 0.359 for Verbal Fluency. Results also varied for the individual subcategories of Inhibition, including a large effect size for decisional impulsivity ($g = 0.817$) and cognitive impulsivity (0.860), and a moderate effect size for motor impulsivity ($g = 0.529$). The Hayling Test, Wisconsin Card Sorting Test, and Iowa Gambling Task were the measures most sensitive for alcohol effects. **Conclusion:** Planning, problem solving, and inhibitory abilities are significantly affected by alcohol abuse, with decisional and cognitive forms of impulsivity most impacted. Cognitive remediation targeting these deficits might increase the related functions that mediate the ability to moderate or abstain from alcohol, and so lead to improved treatment results.

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Introduction

Alcohol use disorder (AUD) has long been associated with cognitive deficits in multiple domains including visuospatial processing, memory, and executive functioning (EF) (1). About half of patients with AUD exhibit cognitive deficits that can significantly influence their treatment compliance and everyday functioning (2), with EF playing an essential role in this process. However, most studies of EF in AUD are based on a methodological assumption that EF is a unitary construct (1). Even when envisioning EF as a single construct, the heterogeneity associated with alcohol damage would likely yield differential impairment (3) depending on such factors as the severity of the disease and length of abstinence. Defective EF can also break down at any stage of the neural circuitry involved in goal-directed activity, possibly involving a cluster of deficiencies with one or two

appearing more prominent than others at any point during the progression of the disease.

Over the past two decades, neuropsychological investigations have increasingly utilized a multidimensional conceptualization of EF (4,5). In addition to lesion and neuroimaging studies suggesting the related but distinct aspects of EF (6,7), studies using exploratory factor analysis have attempted to identify underlying constructs or component processes (5,8,9). Using the Cambridge Neuropsychological Test Automated Battery and the Tower of London Task, Robbins and colleagues (5) found a four-factor solution accounting for 62.2% of the variance. Their derived factors were planning and spatial working memory, attentional set-shifting, strategic aspects of EF, and mnemonic aspects of the spatial working memory. The Shute and Huertas (9) analysis used the Category Test, Wisconsin Card Sort Test (WCST), Trail-Making Test (TMT), Piagetian

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Shadows Task, and Digit Symbol to produce four different factors accounting for 70% of the variance. They showed a strong relationship between operational reasoning and the Category Test, TMT, and WCST. Pineda and Merchan (8) found an additional five factors that accounted for 74.9% of the variance, but only identified the components by the measures loading on each factor. The diversity of these results was likely influenced by the limited number and type of measures included in each study and by relatively small sample sizes.

In the most extensive investigation, Testa and colleagues (10) completed an analysis on 200 adults using 19 clinical neuropsychological tests and arrived at a six-factor solution with weak correlations between measures: 1) Prospective Working Memory, 2) Set-shifting and Interference Management, 3) Task Analysis, 4) Response Inhibition, 5) Strategy Generation and Regulation, and 6) Self-Monitoring and Set-Maintenance. Miyake and colleagues (11) had argued that there is likely a greater unity to executive functions than what may appear in exploratory factor analysis because of the unreliability of EF tests and the “impurity problem,” that is, the issue that each executive test relies on other specific cognitive processes (p. 52). Miyake and his colleagues used confirmatory factor analysis to remove this influence and examined how each of three component processes (shifting, updating, and inhibition) contributed to the performance on several complex executive tasks. Their analysis indicated, nevertheless, that although they shared some underlying commonality, the components were still distinct processes, and show signs of both unity and diversity.

As the purpose of this meta-analysis was to provide clinically relevant information about EF in AUD through the examination of a comprehensive range of standard clinical neuropsychological tests, the empirically derived components from the extensive Testa and colleague’s (10) study appear useful as a general organizing framework. The intention of this study was specifically to analyze the “impure” result; that is, the actual differential process of, for example, “problem solving,” precisely in a form influenced by other subordinate and separate processes as they would occur in actual clinical assessment and treatment conditions. The first and foremost objective was to provide informative test-level effect-size data to clinical neuropsychologists and clinical researchers examining AUD. The second aim was to utilize both previous factor analytical studies and clinical knowledge and usage to summarize the effect size results. Individual tests and measures were assigned to the EF components based on Testa and colleagues’ factors (10), technical data

provided by the test developer or primary studies, and long-standing clinical experience with each test in traditional clinical neuropsychological practice (12). Recognizing the interrelated yet distinct components of EF, and consistent with other recent meta-analyses of EF, test-level data were organized according to the following five subcategories: 1) Planning & Problem Solving, 2) Reasoning & Abstraction, 3) Flexibility & Set Shifting, 4) Verbal Fluency, and 5) Inhibition and Self-Regulation. Although neither mutually exclusive nor comprehensive, these five components of EF are often used in clinical neuropsychological assessments to describe the overarching domains under which commonly used standardized neuropsychological tests are classified (12).

Planning & problem solving

Planning, or the ability to identify and organize the elements and steps necessary to carry out an intention and achieve an objective, requires several executive abilities. One must be able to conceptualize changes into the future, abstractly and practically interact with the environment, make decisions based on weighing conceptualized alternative choices, and maintain ideas related to a structure or conceptual framework for executing the plan (12). This component of EF is similar to Testa and colleagues’ (10) strategy generation and regulation as well as task analysis. An example of two tests where planning and problem-solving figure prominently are the Category Test (13) and California Card Sorting Test (14).

Flexibility & set shifting

The capacity to translate an intention or plan into productive activity depends on the ability to initiate, maintain, switch, and stop sequences of behavior in an orderly and coordinated manner (12). This component of EF best approximates Testa and colleagues’ (10) set-shifting and interference management. Performance on novel activities such as TMT-Part B (15) and WCST (16) are related to this construct.

Reasoning & abstraction

The ability to reason abstractly is required in order to conceptualize or formulate future goals, weigh various possible outcomes, analyze and represent actions into the future, and continually assess and adapt action in relation to intended goals (12). Although this component is not as easily identifiable in pure form in factor analytical studies, it closely resembles Testa and

colleagues' (10) task analysis. This function is highly correlated with performance on tests such as Similarities, Progressive Matrices, and Conceptual Level Analogies Test.

Verbal fluency

This component refers to several abilities related to vocabulary size, lexical access, updating, and inhibition, and is composed of both verbal and executive control functions (17). According to Miyake et al. (11), three aspects of EF can be distinguished in verbal fluency: updating, shifting, and inhibition. Phonological verbal fluency tasks thus require continuous attention to operational criteria, inhibiting or avoiding repetition, cognitive flexibility, and other EF-related abilities.

Inhibition & self-regulation

Impulsivity or the lack of inhibition is generally considered to be action without forethought, conscious judgment, or control. Assessment of self-regulation and inhibitory abilities requires evaluation of productivity and flexibility in confronting and adapting to environmental stimuli (12). An inability to shift a course of thought or action to meet changing demands, resist an impulse, or not automatically react to an environmental stimuli results in perseverative, stereotyped, and non-adaptive impulsive behavior (12). This component is very similar to Testa and colleagues' (10) response inhibition. Inhibition deficits can appear in many tests including the Color-Word Interference Test and the Go/No-Go Test.

Subcategories of impulsivity

Impulsivity has become recognized as a key contributor to several critical phases of drug abuse (18) and to AUD in particular (19). But as is the case with the broader concept of EF, impulsivity is itself not a unitary construct. Item content of the Barratt Impulsivity Scale (20), considered the primary measure for impulsivity in both research and clinical settings (21), reflects Barratt's theory that there are three major subtraits of impulsivity: 1) motor, 2) attentional or cognitive, and 3) decisional or non-planning (22,23). This model has since been statistically explored for its independent components with varying results. In the Patton, Stanford, and Barratt study (24), exploratory principal components analyses suggested six correlated first-order components and three second-order factors consistent with those originally proposed by Barratt.

The three components of the Barratt self-report questionnaire have been shown to correspond with neuropsychological tests for impulsivity. In a sample of ADHD adults and controls, Barratt's motor, non-planning, and attentional deficits of impulsivity related to the corresponding neuropsychological performance in tests such as the Continuous Performance Task and the Iowa Gambling Task. Other studies have demonstrated the interrelatedness between the components of the Barratt Impulsivity Scale and neuropsychological tests such as the Go/NoGo, Continuous Performance Task, WCST, and Iowa Gambling Tasks in pathological gamblers (25), cocaine-dependent individuals (19), and alcohol-dependent subjects (26–28).

The objectives of this study were to examine the effects of alcohol use across these five components of EF and three subcategories of impulsivity in order to determine the functional deficits in each of these domains and the tests that are most sensitive to them using meta-analytical methods.

Method

Search strategies and data acquisition

Three independent investigators (RS, KA, and OA) reviewed 445 potential databases for relevance to the topic. As a result, nine databases were chosen as the most appropriate: 1) PsycINFO, 2) PUBMED, 3) Web of Science, 4) ProQuest Dissertation and Theses, 5) ArticlesFirst, 6) ProceedingsFirst, 7) PapersFirst, 8) CINAHL PLUS, and 9) Academic Search Complete E-Journals. Subsequently, investigators (KA and RS) executed separate searches of each database using their own terms to minimize potential bias in the study collection (see Appendix B).

A specialist with 6 years of professional experience in database searching (OA) created a third independent and extensive search based on a modified version of the PsycINFO database algorithm to pull out all abstracts included in PsycSCAN: Neuropsychology. All searches were then presented to members of the PsycINFO staff for comment and additions, and the feedback received was incorporated. In line with guidelines presented by Grant et al. (29), unique citations were then compiled and discussed for consensus regarding the final list (see Figure 1). The three investigators performed independent searches and identified 5681, 6574, and 5038 abstracts and titles to be further examined. When combined there were 9402 unique citations to be sorted. Two separate investigators then independently rated each citation by title and abstract (if available) and classified them into one of four categories: core, review,

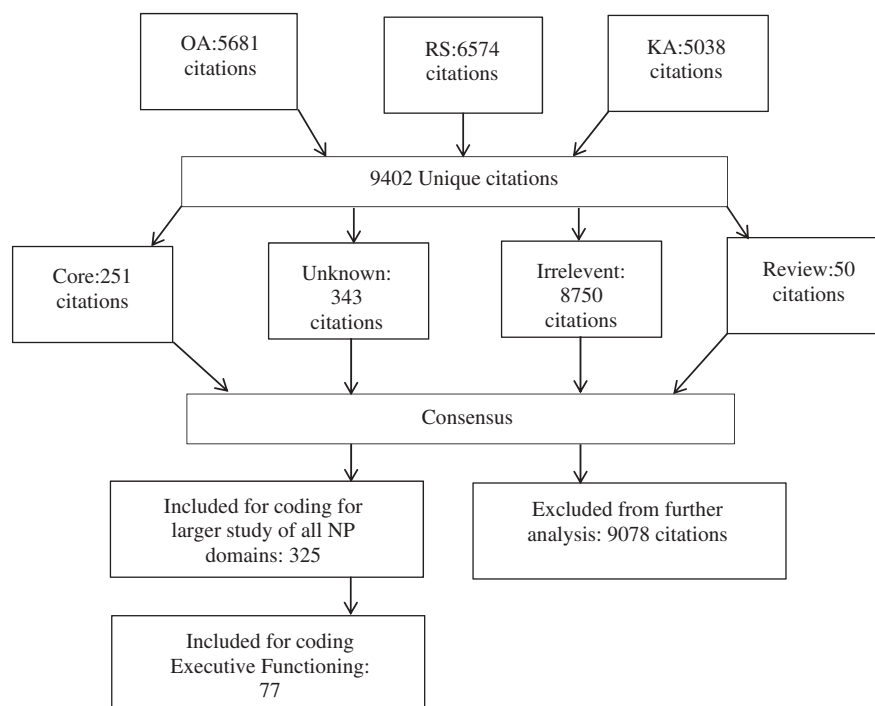


Figure 1. Flowchart of articles through searching, sorting, and consensus.

unknown, and not relevant. The full text articles of all core and unknown citations were examined during consensus meetings and the investigators agreed upon 77 articles that met inclusion criteria. Finally, the reference lists of topic-related meta-analyses, reviews, and primary studies were reviewed to find additional studies. Literature searches were last updated in January, 2015.

Inclusion and exclusion criteria

Research studies included for coding met the following inclusion criteria. The studies have neuropsychological testing as a dependent variable. Participants were identified as adult alcohol-dependent former users. The alcohol group was matched on age and education to a drug-naive comparison group (at the primary study level). This matching could have been done at the group or individual level. Sufficient data were provided to calculate the effect sizes for executive function tests. Studies reported length of abstinence before testing. Alcohol group was drug- and alcohol-free a minimum of 24 hours prior to any neuropsychological testing. Random sampling of alcohol-dependent participants was not required since many studies in the field use convenience samples (e.g., VA hospital inpatients in a substance abuse clinic). Studies excluded comorbid Axis I diagnoses, poly-substance dependence, head trauma, cirrhosis of

the liver, Wernicke's encephalopathy or Korsakoff's syndrome, or other neurological, psychiatric, and other comorbidity that would impact neuropsychological functioning.

Coding procedures

As a result of the database searches, relevance sorting, and the investigator consensus, 325 articles were selected to be included for coding for a larger study examining all neuropsychological domains. Any discrepancies in coding were discussed in a consensus meeting where the original article was referenced to determine the final coding results. Upon consensus, data were transferred into Comprehensive Meta-Analysis Version 2 (CMA) for investigation. Through this coding process, 77 studies were found to include at least one neuropsychological test related to EF. All coding was performed by two independent researchers and any disagreement between the coders was brought to consensus.

Alcohol severity measures and reported length of abstinence were also coded as possible moderators. Independence of investigators was monitored through the searching and coding processes to avoid possible bias (30). Publication bias was controlled by contacting researchers for potential unpublished but relevant data, and analyzed using Duval and Tweedie's trim and fill method (31) and funnel plots.

Effect size statistics and measures of heterogeneity

The Comprehensive Meta-analysis (CMA Version 2.0) statistics software was employed to calculate effect size estimates for Hedges' g , a small sample corrected version of Cohen's d , using a random-effects statistical model. This g is sometimes referred to as g' or g^* because it is the unbiased estimate of the population effect size. Given that Hedges' g is a signed statistic, a positive sign thus corresponds to the higher performance of the healthy control group in comparison to the experimental group. Homogeneity of effect size estimates was assessed using the Q and I^2 statistics. Q is a statistic that is used to assess the ratio of the observed variation to the within-study error (32). The p value associated with the Q statistically tests the null hypothesis that there is no heterogeneity present in the population of effect sizes from which the sample is derived. I^2 can then be used to evaluate the actual proportion of observed variance reflecting real differences in effect sizes (i.e., ratio of true heterogeneity to total observed variation in percentage terms).

Each study in a meta-analysis is permitted to offer only one effect size to the overall analysis. However, this would seriously restrict the amount of information available for use from neuropsychological batteries. When multiple tests were reported by primary studies, composite effect sizes were calculated to avoid the violation of the assumption of independence. These composite effect sizes are the mean effect size within each domain calculated using variance which takes into consideration the correlation among the different tests (32). We expected tests measuring the same EF component to be correlated with each other and corrections were made in the creation of composites. Based on the process used by Grant and colleagues (29), a correlation of 0.7 was used to provide a conservative estimate of variance in the pooled effect size. This value was based on extensive research and neuropsychological experience (29). In addition, sensitivity analyses were used to determine how robust the results were to the violations of assumption of independence. Specifically, sensitivity analyses test the difference between the meta-analysis results when one effect size per study is used (lowest versus highest effect size from each study) and when all effects sizes are used (violating the assumption of independence). These in turn can be compared to the use of composites (which avoid the violation of independence). To our knowledge, sensitivity analyses have never been used in neuropsychology meta-analytical research before, but are the accepted state-of-the-art technique in testing this assumption in meta-analysis (32). Finally, funnel plots and Duval and Tweedie's Trim and Fill (31) were used to examine publication bias. Due to the richness of the data, most results are presented as tables that allow clinical neuropsychologists and other

professionals to evaluate the tests they might want to employ in assessing AUD patients in each domain of EF.

Similar to other neuropsychological meta-analyses (33,34), we used the typical benchmarks to describe the magnitude of effect sizes proposed by Cohen (35). These are 0.2, 0.5, and 0.8, which correspond to small, medium, and large, respectively. The qualitative descriptors proposed by Cohen (35) were adopted for the purposes of providing the reader with verbal anchor points for understanding the numerical values. Although this is not a perfect method for interpreting the magnitude of effect sizes, it has been used for so long that it provides a familiar benchmark to the reader. Other techniques to evaluate these effect sizes have been proposed by Durlak (36); however, using multiple methods to describe the results are beyond the scope of this meta-analysis.

Results

A total of 77 studies were selected for analysis with 2576 healthy comparison subjects and 2620 subjects with AUD (see Table 1 for demographic and other characteristics). The overall summary Hedges' g effect size for all EF measures from all 77 studies was 0.643 (95% CI [0.561–0.724], $z = 15.452$, $df = 153$, $p < 0.000$), a moderate effect size with medium heterogeneity ($I^2 = 74.067$, $Q = 589.981$, $df = 153$, $p < 0.000$) generally consistent with previous studies.

Test-level meta-analyses

Except for Semantic Verbal Fluency and Similarities, most tests demonstrated statistically significant effect sizes that range from 0.34 to 1.44 (see Table 2). The Hayling Test and the number of categories and errors on the WCST demonstrated the largest effect sizes. In addition, the Iowa Gambling Task, Cognitive Estimate Test, and Category Test demonstrated large effect sizes.

Composite level meta-analyses

All five composites were statistically significant for effect size and for heterogeneity (see Tables 3 and 4). The Hedges' g value for the Inhibition & Self-Regulation composite was 0.803 (95% CI [0.572–1.034], $z = 6.818$, $df = 25$, $p < 0.000$), the largest effect size of all the EF composites. The Planning & Problem Solving composite had the second highest effect size (see Table 3). Flexibility & Set Shifting composite had a moderate effect size, while the Reasoning & Abstraction and Verbal Fluency composites had small effect sizes. An analysis of the heterogeneity (Q)

Table 1. Summary of included studies and sample characteristics.

Studies	Functions assessed	Neuropsychological tests	Healthy controls (n)	Mean age of healthy controls	Mean education of healthy controls	Males in control group (%)	Alcohol users (n)	Mean age of alcohol users	Mean education of alcohol users	Males in alcohol group (%)	Mean duration of use (years)	Mean length of abstinence (days)
Acker, 1984	Flexibility	Category Test	90	39.3	11.8	—	92	41.7	10.5	69.9	10.5	13.6
Beatty, 1993	Inhibition, Planning, Reasoning	WCST, California Card Sorting Test, Conceptual Level Analogies Test, Shipley Abstracting	16	36.8	13.6	56.25	23	38.8	13	60.87	11.4	30
Beatty, 1995	Inhibition, Planning, Reasoning, Flexibility	TMT B, WCST, Shipley Abstracting, Conceptual Level Analogies Test	22	35.5	14	59.09	24	38.6	12.8	66.67	11.4	14
Chanraud, 2007	Inhibition, Planning, Flexibility	TMT B, Letter Number Sequencing, Verbal Fluency, Stroop Interference, WCST	24	45	8.7	100	26	47.7	7.58	100	8	184.8
Chmielowski, 1980	Executive Function	Luria-Nebraska Intelligence	40	47.52	11.54	100	40	50.24	11.24	100	—	17.5
Claiborn, 1981	Flexibility	TMT B	25	26.68	13.04	100	25	44.84	11.96	100	10	14
Davies, 2005	Flexibility	TMT B, Verbal Fluency	58	43	—	70.68	43	43.7	—	79.07	—	157.5
De Obaldia, 1981	Executive Function	Luria-Nebraska Intelligence	15	45.46	12.13	100	30	45.8	11.8	100	12.46	21
De Sousa Uva, 2010	Inhibition, Flexibility	TMT B, TMT B-A, Iowa Gambling Test, Stroop Interference	22	44.36	—	63.63	35	48.4	—	48.5	—	—
Demir, 2002	Inhibition, Planning, Flexibility	WCST, Verbal Fluency	6	40	11	100	13	41.15	9.76	100	—	18
Di Scalfani, 1995	Flexibility, Reasoning	TMT B, Shipley Abstracting	11	63	16.7	100	14	59.7	15	100	26.6	10.3
Durazzo, 2013	Executive Function	Executive Function Domain	39	48	15.7	85	30	52	14.4	87	19.33	33
Easton, 2008	Composite Inhibition, Planning, Flexibility	TMT B, Continuous Performance Test, Iowa Gambling Test, Stroop Interference, WCST	7	—	—	100	9	—	—	100	—	14
Errico, 1991	Flexibility	Verbal Fluency	30	35.7	13.1	100	50	38.1	12.7	100	14.6	32
Errico, 2002	Inhibition	WCST	30	37	13	100	48	39.2	12.9	100	—	32
Fabian, 1983	Planning, Flexibility, Reasoning	TMT B, Category Test, Shipley Abstracting	70	42.34	13.06	0	40	42.15	12.88	0	6.38	21
Fallgatter, 1998	Inhibition	Go/No-Go	20	40.8	—	80	20	44.1	—	80	—	10
Fama, 2004	Inhibition, Planning	WCST	63	45.7	16.2	100	51	43.2	13.2	100	—	25
Glenn, 1991	Planning	Bexley-Maudsley Category Sorting Test	36	32.6	13	0	48	32.8	12.3	0	10.4	32
Goldstein, 1965	Inhibition, Flexibility	TMT B Time, Stroop Interference	50	41.84	12.72	100	50	44.76	10.98	100	—	14
Goldstein, 2001	Inhibition	Stroop Interference	17	35.1	13	100	17	38.7	12.4	100	10	—
Goudriaan, 2006	Inhibition, Planning, Flexibility	Verbal Fluency, Circle Tracing, Stop Signal Reaction, Stroop Interference, WCST, Tower of London	48	35.6	—	72.92	50	47.2	—	74	11.2	—
Grant, 1979	Planning, Flexibility	TMT B, Category Test	40	37	13	100	43	36.8	12.6	100	—	21
Gudeman, 1977	Inhibition, Planning, Flexibility, Reasoning	Color Screen Test, TMT B, Color-Word Confusion Test, Category Test, Similarities	41	44.3	14.1	65.85	41	45.2	13.6	65.85	9.59	21.37
Hildebrandt, 2004	Flexibility, Reasoning	Verbal Fluency	40	51	—	100	24	52	—	100	17	14
Hill, 1980	Planning	Category Test Errors	12	28	12.7	100	15	34.3	11	—	14.3	—
Hochla, 1982	Planning, Flexibility, Reasoning	TMT B, Category Test, Similarities	35	44.9	13.17	0	35	44.2	13.16	0	5.75	34.17
Jenkins, 1979	Inhibition, Planning, Reasoning	WCST, Shipley Abstracting	24	45.96	12.48	100	24	44.54	11.5	100	12.87	18
Jones, 1972	Planning, Reasoning	Category Test, Shipley Abstracting	26	46.92	12.42	100	26	46.54	11.81	100	27.46	38.62
Joyce, 1991	Planning, Flexibility	Verbal Fluency, Category Test, WCST	22	55.6	—	72.73	22	53.4	—	90.91	20.38	180
Kim, 2011	Inhibition, Planning	Iowa Gambling Test, WCST	21	30.52	15.14	100	23	32.65	11.26	100	4.91	14

(Continued)

Table 1. (Continued).

Studies	Functions assessed	Neuropsychological tests	Healthy controls (n)	Mean age of healthy controls	Mean education of healthy controls	Males in control group (%)	Alcohol users (n)	Mean age of alcohol users	Mean education of alcohol users	Males in alcohol group (%)	Mean duration of use (years)	Mean length of abstinence (days)
Konrad, 2012	Inhibition, Planning, Flexibility	TMT B, Stroop Interference, WCST	23	47.4	—	100	24	48.5	—	100	14.1	13
Krabbendam, 2000	Inhibition, Flexibility	Concept Shifting Test, Verbal Fluency, Stroop Interference	16	46.9	11.4	81.25	15	46.7	10.9	80	17.5	30
Loeber, 2009	Inhibition, Planning, Flexibility	TMT B, Iowa Gambling Test, WCST	36	44.4	—	63.89	48	46.5	—	56.25	—	15.65
Long, 1974	Planning, Flexibility, Reasoning	TMT B, Category Test, Similarities	22	45.86	14.32	100	22	44.64	13.86	100	21.55	11.41
Mallick, 1993	Flexibility	Verbal Fluency	20	31.3	10.7	100	20	33.05	9.95	100	12.35	14
Mann, 1999	Flexibility, Reasoning	TMT B, Verbal Fluency, Reasoning	63	41.8	—	0	49	41.7	—	100	11.4	17.8
Moriyama, 2002	Executive Function	BADS, TMT B	15	51.6	12.5	100	22	51.6	12.5	100	26.7	51.4
Munro, 2000	Composite, Planning, Flexibility, Reasoning	TMT B, Verbal Fluency	17	66.94	13.27	52.94	18	64	11.56	94.44	—	90.52
Nixon, 1992	Flexibility	Problem Solving Composite, TMT B	36	—	—	100	48	—	—	100	16.4	21
Nixon, 1996	Executive Function	TMT B Time	13	33.85	13	53.85	13	38	12.69	69.23	14.31	31
Noel, 2001	Flexibility	Flexibility Test, Stroop Interference, TMT B, Verbal Fluency, Hayling Test, Brixton Test	30	42.7	12.9	100	30	43.1	12.4	100	14.4	138.6
Noel, 2007	Inhibition, Planning	Hayling Test, Brixton Test	30	44.1	10.8	63.33	30	45.8	10.7	66.67	14.05	135.1
Noel, 2009	Inhibition	Directed Forgetting Task	26	51.4	13.7	65.38	38	49.3	13.7	65.79	10.4	22
Noel, 2011	Inhibition	Hayling Test	30	44.1	10.8	60	30	45.8	10.7	60	17.05	19.3
Noel, 2013	Inhibition	Hayling Test, Stroop Interference	30	44.04	12.53	76.67	30	43.34	12.5	76.67	10.43	20.9
O'Leary, 1977	Flexibility	TMT B	20	49.9	12.9	100	24	51	12.2	100	—	11
O'Leary, 1979	Flexibility, Planning, Reasoning	TMT B, Category Test, Similarities	38	49.9	12.9	100	38	49.8	12.6	100	—	14
Oscar-Berman, 2004	Inhibition, Flexibility, Planning	Ruff Figural Fluency Test, TMT B, Verbal Fluency, WCST, Progressive Planning Test	82	52.2	15.6	41.46	50	51.6	14.6	66	—	49.7
Pitel, 2007	Inhibition, Flexibility	Verbal Fluency, Stroop Interference	20	48.4	11.4	—	20	47.2	9.9	—	21.8	14
Pitel, 2009	Inhibition, Flexibility, Reasoning	Alternate Response, Verbal Fluency, Stroop Interference, Integration Test	54	48.68	10.56	—	14	47.05	10.36	—	9.75	6.39
Ratti, 1999	Flexibility	Verbal Fluency, Progressive Matrices	15	—	—	100	15	50.7	7.5	100	22.5	—
Ratti, 2002	Inhibition, Flexibility, Planning	TMT B, TMT B-A, Stroop Interference, WCST	22	—	—	100	22	51.6	7.7	100	16.6	—
Reed, 1992	Flexibility, Planning	TMT B, Category Test	37	48.2	14.2	100	31	45.9	14	100	15.7	29.2
Ron, 1983	Inhibition, Flexibility, Planning	TMT B, Verbal Fluency, WCST	50	41.5	—	100	100	43.5	—	100	17.3	39.1
Rourke, 1999	Flexibility, Planning	TMT B, Category Test	49	49.9	14.4	100	97	48.4	13.6	100	17.2	29.7
Rupp, 2006	Inhibition, Planning	WCST	30	45.3	10	53.33	32	44.6	9.5	56.25	9.3	35
Rustemeier, 2012	Inhibition	Go/No-Go	20	45.95	—	0	24	45.17	—	0	10.12	6
Salgado, 2009	Inhibition	Continuous Performance Task, Iowa Gambling Test, WCST	30	46.93	11.07	66.67	31	48.97	10.55	83.87	10	15
Sassoon, 2007	Flexibility	Color Trails	49	41.1	14.9	55.1	44	43.4	13.4	61.36	—	273
Saxton, 2000	Flexibility, Planning	TMT B, Verbal Fluency, WCST	15	70.8	13.2	53.33	29	64.5	12.2	89.65	43.9	—
Schaeffer, 1986	Flexibility, Planning, Reasoning	TMT B, Booklet Category Test, Levine Hypothesis Test, Conceptual Level Analogies Test, Shipley Abstracting	43	38	122.8	100	60	39.9	12.6	100	11.3	31.4

(Continued)

Table 1. (Continued).

Studies	Functions assessed	Neuropsychological tests	Healthy controls (n)	Mean age of healthy controls	Mean education of healthy controls	Males in control group (%)	Alcohol users (n)	Mean age of alcohol users	Mean education of alcohol users	Males in alcohol group (%)	Mean duration of use (years)	Mean length of abstinence (days)
Schaeffer, 1989	Planning, Reasoning	Levine Hypothesis Test, Conceptual Level Analogies Test	15	43.4	12.8	100	20	43.8	12.7	100	16.2	21
Scheurich, 2004	Flexibility	TMT B	59	43	10.8	100	57	45.5	10.6	100	1	9
Shelfton, 1984	Reasoning	Shipley Abstracting	36	42.5	12.8	100	36	42.4	13	100	11.7	21
Silberstein, 1979	Inhibition, Flexibility, Planning, Reasoning	TMT B, WCST, Category Test, Shipley Abstracting, Similarities	25	42	12.6	0	25	42	12.38	0	6.56	28.76
Smith, 2010	Inhibition, Flexibility, Planning, Reasoning	TMT B, Verbal Fluency, Stroop Interference, Short Category Test, Microcog Analogies, Microcog Object Match	33	32.25	16.53	100	33	32.32	16.36	100	—	—
Stretter, 1995	Inhibition	Stroop Interference	40	34	—	100	40	35.4	—	100	8	13.7
Tarquini, 1981	Flexibility, Planning, Reasoning	Verbal Fluency, Temporal Rules Induction, Simple Analogies Test	83	—	—	—	28	—	—	78.57	16.4	14
Tomassini, 2012	Inhibition	Iowa Gambling Test	24	40.08	12.37	54.17	27	46.15	9.38	77.78	2	16.85
Turner, 1988	Planning, Reasoning	Booklet Category Test, Levine Hypothesis Test, Conceptual Level Analogies Test, Shipley Abstracting	48	35.6	13.1	0	54	35.1	13.3	0	8.6	—
Uekermann, 2003	Flexibility, Reasoning	Verbal Fluency, Cognitive Estimate Test, Similarities	28	42.32	17	60.71	30	42.6	—	60	7.87	61.38
Uekermann, 2006	Inhibition, Flexibility	TMT B, Stroop Interference	29	42.69	—	65.52	29	41.79	—	79	14	75
Wagman, 1980	Inhibition, Planning	WCST	25	30	—	100	30	35.4	—	100	—	14
Wolf, 1979	Planning	Category Test	12	28	12.7	100	15	34.3	11	100	14.3	30
Yohman, 1985	Inhibition, Planning, Reasoning	WCST, Ravens Matrices, Shipley Abstracting	20	46.2	12.9	100	37	48	12.4	100	13.4	35
Yohman, 1987	Reasoning	Conceptual Level Analogies Test	60	40.2	12.7	100	60	39.9	12.5	100	11.3	31.4

Note: n = Number of participants, WCST = Wisconsin Card Sorting Test, TMT = Trail Making Test, BADS = Behavioral Assessment of the Dysexecutive Syndrome. See Appendix A for bibliography of all included studies.

Table 2. Meta-analytical results for individual executive functioning tests.

Executive Functioning Test	Effect size estimates					Test of heterogeneity				
	<i>k</i>	Alcohol (<i>n</i>)	Control (<i>n</i>)	<i>g</i> (SE)	95% CI	<i>z</i>	<i>p</i>	<i>I</i> ²	<i>Q</i>	<i>p</i>
Hayling Test	3	90	90	1.437 (0.352)	0.746 to 2.128	4.078	<0.000	76.5	8.511	0.014
WCST Categories	16	463	401	1.069 (0.248)	0.583 to 1.554	4.315	<0.000	90.665	160.68	~0
WCST Errors	10	311	249	0.877 (0.133)	0.617 to 1.137	6.612	<0.000	51.192	18.44	0.03
Iowa Gambling Task Total Score	6	156	140	0.817 (0.210)	0.406 to 1.228	3.895	<0.000	64.734	14.178	0.015
Cognitive Estimate Test	3	82	63	0.719 (0.172)	0.382 to 1.055	4.185	<0.000	~0	0.571	0.752
Category Test	13	542	506	0.646 (0.070)	0.509 to 0.782	9.278	<0.000	~0	11.217	0.51
WCST Perseverative Errors	15	511	384	0.645 (0.081)	0.487 to 0.804	7.966	<0.000	23.361	18.267	0.195
WCST Perseverative Responses	5	179	219	0.603 (0.216)	0.179 to 1.027	2.79	0.005	75.25	16.162	0.003
Trail Making Test B	34	1250	1175	0.593 (0.055)	0.485 to 0.702	10.715	<0.000	39.59	54.627	0.01
Conceptual Level Analogies Test	6	241	204	0.539 (0.096)	0.350 to 0.727	5.591	<0.000	~0	4.429	0.489
Shipley Abstracting Test	11	363	341	0.519 (0.077)	0.368 to 0.669	6.739	<0.000	~0	9.98	0.442
Levine Hypothesis Test	3	134	106	0.485 (0.131)	0.229 to 0.742	3.705	<0.000	~0	1.216	0.544
Analogies (MICROCOG)	3	85	68	0.450 (0.221)	0.018 to 0.883	2.039	0.041	41.942	3.445	0.179
WCST Non-Perseverative Errors	3	78	71	0.391 (0.164)	0.071 to 0.712	2.392	0.017	~0	1.6	0.449
Stroop Color-Word Test	17	474	495	0.358 (0.654)	0.312 to 0.796	6.698	<0.000	22.411	20.621	0.194
Verbal Fluency Phonological	20	666	748	0.340 (0.091)	0.162 to 0.518	3.748	<0.000	60.535	48.143	~0
Verbal Fluency Semantic	7	191	164	0.293 (0.160)	-0.020 to 0.606	1.834	0.067	51.335	12.329	0.05
Similarities	6	191	189	0.194 (0.010)	-0.005 to 0.394	1.912	0.056	~0	1.702	0.889

Note: *k* = number of comparisons, *n* = sample size, *g* = Hedges *g* effect size, SE = standard error, CI = confidence interval, *z* = *z* score, *p* = significance level, *I*² = percentage of total variance, *Q* = variance between studies as a proportion of total variance, WCST = Wisconsin Card Sorting Test.

Table 3. Overall executive functioning composite and its subcategories.

Executive Functioning Test	Effect size estimates					Test of heterogeneity					
	<i>k</i>	Alcohol (<i>n</i>)	Control (<i>n</i>)	<i>g</i> (SE)	95% CI	<i>z</i>	<i>p</i>	<i>I</i> ²	<i>Q</i>	<i>df</i>	<i>p</i>
Executive Function Summary	154	5140	5153	0.643 (0.042)	0.561 to 0.724	15.452	<0.000	74.067	589.981	153	<0.000
Flexibility and Set Shifting	45	1559	1483	0.663 (0.071)	0.525 to 0.802	9.375	<0.000	69.723	145.326	44	<0.000
Trail Making Test B	34	1250	1175	0.593 (0.055)	0.485 to 0.702	10.715	<0.000	39.59	54.627	33	0.01
Trail Making Test B - A	2	57	44	0.611 (0.439)	-0.250 to 1.472	1.392	0.164	77.621	4.469	1	0.035
Color Screen Test	1	41	41	0.551 (0.223)	0.114 to 0.988	2.473	0.013	—	—	—	—
Concept Shifting Test	1	15	16	0.063 (0.350)	-0.623 to 0.749	0.180	0.857	—	—	—	—
BADS Rule Shift Card	1	22	15	1.490 (0.371)	0.763 to 2.216	4.02	<0.000	—	—	—	—
Flexibility Test	1	30	30	0.448 (0.258)	-0.058 to 0.953	1.734	0.083	—	—	—	—
Stroop Flexibility	1	30	30	0.958 (0.269)	0.430 to 1.487	3.557	<0.000	—	—	—	—
Ruff Figural Fluency Test	1	50	82	0.088 (0.178)	-0.262 to 0.438	0.494	0.621	—	—	—	—
Alternate Response	1	14	54	0.250 (0.297)	-0.333 to 0.833	0.840	0.401	—	—	—	—
WCST Perseverative Errors	15	511	384	0.645 (0.081)	0.487 to 0.804	7.966	<0.000	23.361	18.267	14	0.195
Reasoning and Abstraction	24	770	843	0.479 (0.069)	0.344 to 0.614	6.95	<0.000	42.063	39.698	23	0.017
Conceptual Level Analogies Test	6	241	204	0.539 (0.096)	0.350 to 0.727	5.591	<0.000	<0.000	4.429	5	0.489
Shipley Abstracting Test	11	363	341	0.519 (0.077)	0.368 to 0.669	6.739	<0.000	<0.000	9.98	10	0.442
Similarities	6	191	189	0.194 (0.010)	-0.005 to 0.394	1.912	0.056	<0.000	1.702	5	0.889
Reasoning	1	49	63	0.276 (0.190)	-0.096 to 0.649	1.455	0.146	—	—	—	—
BADS Temporal Judgement	1	22	15	0.128 (0.328)	-0.514 to 0.771	0.392	0.695	—	—	—	—
Integration Test	1	14	54	0.607 (0.302)	0.015 to 1.198	2.011	0.044	—	—	—	—
Progressive Matrices	2	52	35	0.686 (0.223)	0.249 to 1.124	3.076	0.002	<0.000	0.52	1	0.471
Analogies (Microcog)	3	85	68	0.450 (0.221)	0.018 to 0.883	2.039	0.041	41.942	3.445	2	0.179
Cognitive Estimate Test	3	82	63	0.719 (0.172)	0.382 to 1.055	4.185	<0.000	<0.000	0.571	2	0.752
Planning and Problem Solving	39	1358	1300	0.773 (0.102)	0.574 to 0.972	7.612	<0.000	82.945	222.813	38	<0.000
Category Test	13	450	429	0.646 (0.070)	0.509 to 0.782	9.278	<0.000	<0.000	11.217	12	0.51
California Card Sorting Test	1	23	16	1.181 (0.350)	0.494 to 1.867	3.369	0.001	—	—	—	—
WCST Categories	16	463	401	1.069 (0.248)	0.583 to 1.554	4.315	<0.000	90.665	160.68	15	<0.000
Bexley-Maudsley Category Sorting Test	1	48	36	0.068 (0.219)	-0.360 to 0.496	0.310	0.756	—	—	—	—
Tower of London	1	50	48	0.626 (0.205)	0.223 to 1.028	3.045	0.002	—	—	—	—
BADS Action Program	1	22	15	0.539 (0.334)	-0.115 to 1.192	1.615	0.106	—	—	—	—
BADS Key Search	1	22	15	0.981 (0.347)	0.301 to 1.661	2.828	0.005	—	—	—	—
BADS Modified Six Elements	1	22	15	1.580 (0.376)	0.844 to 2.316	4.206	<0.000	—	—	—	—
BADS Zoo Map	2	60	60	0.954 (0.546)	-0.116 to 2.023	1.748	0.081	87.39	7.93	1	0.005
Brixton Test	1	50	82	0.141 (0.179)	-0.209 to 0.491	0.788	0.43	—	—	—	—
Progressive Planning Test	2	114	91	0.586 (0.143)	0.306 to 0.866	4.098	<0.000	33.221	1.497	1	0.221
Booklet Category Test	3	134	106	0.485 (0.131)	0.229 to 0.742	3.705	<0.000	<0.000	1.216	2	0.544
Levine Hypothesis Test	1	33	33	0.019 (0.243)	-0.458 to 0.496	0.079	0.937	—	—	—	—
Short Categories Test	1	28	83	0.101 (0.217)	-0.325 to 0.526	0.465	0.642	—	—	—	—
Verbal Fluency	20	666	748	0.359 (0.078)	0.206 to 0.512	4.596	<0.000	47.156	35.957	19	0.011
Phonemic Fluency	20	666	748	0.359 (0.078)	0.206 to 0.512	4.596	<0.000	47.156	35.957	19	0.011

Note: *k* = number of comparisons, *n* = sample size, *g* = Hedges *g* effect size, SE = standard error, CI = confidence interval, *z* = *z* score, *p* = significance level, *I*² = percentage of total variance, *Q* = variance between studies as a proportion of total variance, *df* = degrees of freedom, BADS = Behavioral Assessment of the Dysexecutive Syndrome, WCST = Wisconsin Card Sorting Test.

Table 4. Overall inhibition composite and its subcategories.

	Effect Size Estimates					Test of Heterogeneity					
	<i>k</i>	Alcohol (<i>n</i>)	Control (<i>n</i>)	<i>g</i> (<i>SE</i>)	95% <i>CI</i>	<i>z</i>	<i>p</i>	<i>I</i> ²	<i>Q</i>	<i>df</i>	<i>p</i>
Inhibition & Self-Regulation	26	739	743	0.803 (0.119)	0.572 to 1.034	6.818	<0.000	77.417	110.703	25	<0.000
Inhibition: Motor Composite	3	83	75	0.529 (0.160)	0.214 to 0.643	3.297	0.001	00.000	1.136	2	0.567
CPT Commission Errors	1	9	7	0.094 (0.477)	-0.841 to 1.028	0.196	0.844	—	—	—	—
Go/No Go False Alarms	1	24	20	0.697 (0.306)	0.097 to 1.298	2.275	0.023	—	—	—	—
Stop Signal Reaction Time	1	50	48	0.750 (0.208)	0.343 to 1.156	3.613	<0.000	—	—	—	—
Circle Tracing Time	1	50	48	0.317 (0.202)	-0.078 to 0.713	1.572	0.116	—	—	—	—
Inhibition: Decisional Composite	6	156	140	0.817 (0.210)	0.406 to 1.228	3.895	<0.000	64.734	14.178	5	0.015
Iowa Gambling Task Total Score	6	156	140	0.817 (0.210)	0.406 to 1.228	3.895	<0.000	64.734	14.178	5	0.015
Inhibition: Cognitive Composite	21	607	612	0.860 (0.143)	0.580 to 1.141	6.013	<0.000	80.959	105.035	20	<0.000
Stroop Color-Word Test	16	444	465	0.478 (0.074)	0.333 to 0.624	6.438	<0.000	15.167	17.682	15	0.28
Color-Word Confusion Test	1	41	41	0.464 (0.222)	0.029 to 0.898	2.092	0.036	—	—	—	—
Go/No-Go Reaction Time	1	24	20	0.029 (0.088)	-0.554 to 0.611	0.096	0.924	—	—	—	—
Hayling Test	3	90	90	1.437 (0.352)	0.746 to 2.128	4.078	<0.000	76.5	8.511	2	0.014
Directed Forgetting Task	1	38	26	0.727 (0.260)	0.218 to 1.235	2.801	0.005	—	—	—	—

Note: *k* = number of comparisons, *n* = sample size, *g* = Hedges *g* effect size, *SE* = standard error, *CI* = confidence interval, *z* = *z* score, *p* = significance level, *I*² = percentage of total variance, *Q* = variance between studies as a proportion of total variance, *df* = degrees of freedom, BADS = Behavioral Assessment of the Dysexecutive Syndrome, WCST = Wisconsin Card Sorting Test, CPT = Continuous Performance Task, RFF = Ruff Figural Fluency.

indicated that all the composites had significant heterogeneity in the moderate range.

Inhibition & self-regulation

A third analysis of this study examined the effect sizes of three subcategories of impulsivity (see Table 4). All three subcategories were statistically significant for effect sizes. The Hedges' *g* value for the Cognitive subcategory was 0.860 (95% CI [0.580–1.141], *z* = 6.013, *df* = 20, *p* < 0.000) and for the Decisional subcategory 0.817 (95% CI [0.406–1.228], *z* = 3.895, *df* = 5, *p* < 0.015), both large effect sizes. The Motor subcategory had a moderate effect size of 0.529 (95% CI [0.214–0.643], *z* = 3.297, *df* = 2, *p* = 0.001).

Sensitivity and subgroup analysis

Results of the subgroup analysis for EF using a mixed effects model showed an overall significant statistical difference between the five composites ($Q_B = 18.633$, *df* = 4, *p* = 0.001) but not between the subcategories of impulsivity ($Q_B = 1.995$, *df* = 2, *p* = 0.369). A *post hoc* pairwise comparison showed a statistically significant difference between Inhibition & Self-Regulation and Reasoning & Abstraction ($Q_B = 5.625$, *df* = 1, *p* = 0.018), between Planning & Problem Solving and Reasoning & Abstraction ($Q_B = 5.722$, *df* = 1, *p* = 0.017), between Planning & Problem Solving and Verbal Fluency ($Q_B = 10.414$, *df* = 1, *p* = 0.001), between Flexibility & Set Shifting and Verbal Fluency ($Q_B = 8.311$, *df* = 1, *p* = 0.004), and between Inhibition & Self-Regulation and Verbal Fluency ($Q_B = 9.849$, *df* = 1, *p* = 0.002). The influence of any violation of independence in the EF composite was assessed by a sensitivity analysis performed by selecting the highest and

lowest effect size from each study in each composite. Heterogeneity remained consistent across subgroups and so indicated a lack of influence from potential violations of independence on the values for statistical significance. Similar tests were performed with impulsivity composites with similar results.

Risk of publication bias

Using the Duval and Tweedie trim and fill method with a random effects model (31,32,37), the overall moderate effect size result for all 77 studies in this meta-analysis (*g* = 0.569) was found to be robust against potential overestimation bias (see Figure 2). Using the same method to examine all other domains, the only effect size overestimation detected was in Verbal Fluency (biased estimate of *g* = 0.359 and unbiased estimate of *g* = 0.303; see Figure 3).

Discussion

As hypothesized, estimated effect sizes across the neuropsychological tests for EF fell primarily in the large and moderate effect-size ranges. The tests demonstrating the least sensitivity to alcohol effects were Similarities, Verbal Fluency, and the Stroop Color-Word Interference Test, while many tests frequently used to assess EF deficits in alcohol research (Conceptual Level Analogies Test, Levine Hypothesis Test, Shipley Abstracting Test, and TMT B) were only moderately sensitive. The low sensitivity of Similarities and Verbal Fluency Tests were consistent with a relatively more preserved verbal ability, an early and consistent finding in alcohol research. The WCST, especially the Categories and Error scores, was highly sensitive to alcohol effects, consistent with its

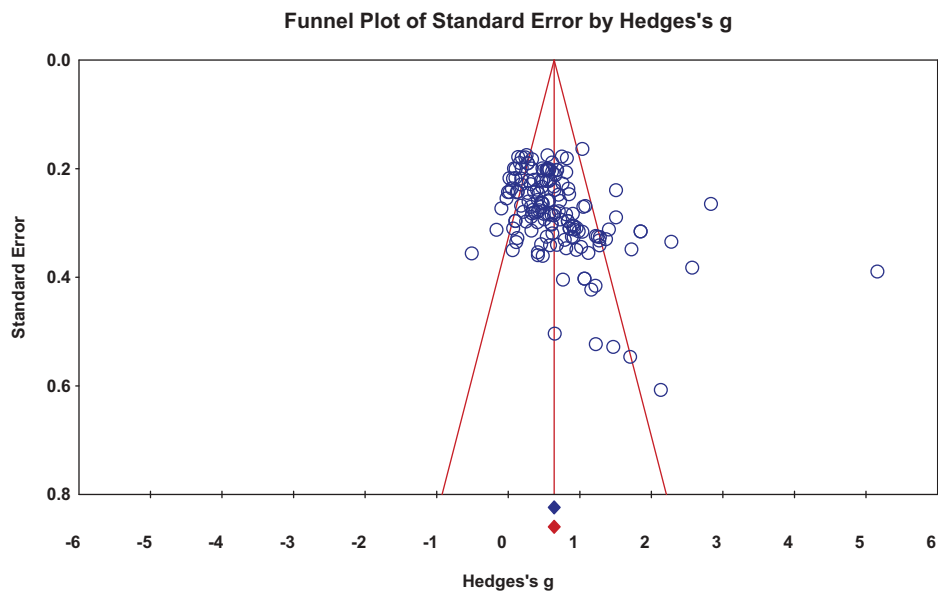


Figure 2. Overall executive functioning publication bias funnel plot showing no overestimation bias.

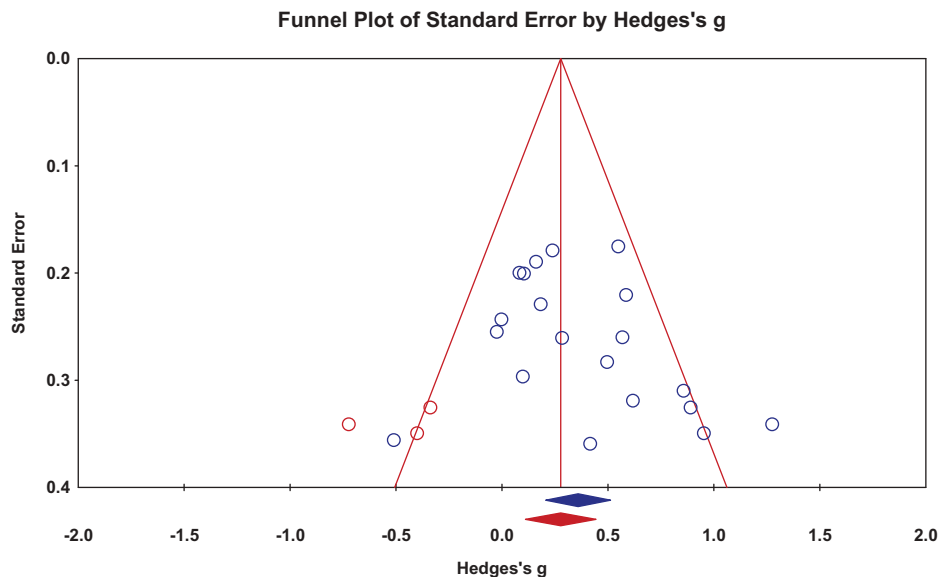


Figure 3. Verbal fluency publication bias funnel plot showing a slight overestimation bias corrected for by fill and trim method.

traditional use as a measure of frontal lobe damage (12). Indeed, the four most sensitive neuropsychological tests for EF were the Iowa Gambling Task, Categories and Errors from the WCST, and the Hayling Test.

The Iowa Gambling Task (38) uses four decks of cards with different awards and penalties to simulate real-life decision-making. Alcohol-abusing subjects are impulsively driven by immediate rewards rather than the future consequences of their actions. The WCST (39) measures several cognitive abilities related to identifying abstract categories, sorting stimuli according to these dimensions, and shifting approaches based on

environmental feedback. According to Barcelo and Knights (40) study, lower performance on the category score on the WCST can reflect an error related to a deficiency in problem solving, an inability to shift set, or an inability to maintain a set due to a disinhibited interference. Thus, it measures perseverative as well as random errors, and relies on inhibitory abilities as well as reasoning, planning, problem solving, and flexibility. Its high sensitivity to alcohol damage likely rests on this breadth of incorporated functions including inhibition.

The most sensitive instrument based on three studies, the Hayling Test (41), is a classic assessment of the ability to suppress a prepotent response, and so

functions as a measure of inhibitory abilities. Two sections of the test present 15 sentences with a missing last word. In the first section, subjects are asked to say a word that correctly completes the sentence. In the second section, subjects are asked for a word that would not correctly complete the sentence and would be unconnected to the sentence. In this way, subjects have to first suppress or inhibit a powerfully activated response before they could say a new unconnected one.

Although the WCST has been a traditional measure used in alcohol research, the Hayling Test and Iowa Gambling Task have been used far less frequently. By including these sensitive tests for EF, future studies may more accurately reflect the extent of the cognitive deficits in detoxified subjects with AUD.

Composites and overall effects in EF

In their meta-analytic study, Stavro, Pelletier, and Potvin (1) reported for short-term abstinent subjects an effect size of $g = 0.534$ for problem solving/EFs and an effect size of $g = 0.460$ for inhibition/impulsivity. Those findings are inconsistent with the results of the current study.

With a large rather than small effect size estimate for the Inhibition & Self-Regulation composite ($g = 0.803$), the current investigation suggests that inhibition is more severely affected than presented in the Stavro and colleague study (1). Further, the current study revealed a larger effect size for the Planning & Problem Solving composite ($g = 0.773$). In the previous study, the overall moderate effect size for EF likely resulted from combining the lower effect size found in the Reasoning & Abstraction, Flexibility & Set Shifting, and Verbal Fluency domains with the higher effect in Planning & Problem Solving.

In the current study, there was consistency within the finding of large reductions in inhibitory ability relative to healthy comparison groups. Both the neuropsychological test analysis and the composite-level analysis suggest that this ability is severely affected. Inhibitory functions—especially decisional and cognitive impulsivity, the subcategories with the largest effect—have been associated more with the orbitofrontal cortex or the ventromedial prefrontal cortex, and the dorsolateral prefrontal cortex has been more associated with Planning & Problem Solving (42–46). Damaged orbitofrontal areas have been specifically linked to the excessive drive and compulsion experienced in alcohol abuse and other forms of addiction, symptoms likely resulting from dysfunction of reward circuitry controlling motivation, reward, and impulsivity (44,47,48).

Current findings appear consistent with a vulnerability to both the orbitofrontal cortex and the dorsolateral prefrontal cortex and their associated neuronal circuitry.

Cognitive remediation in alcohol abuse treatment

Distinguishing Planning & Problem Solving and Decisional and Cognitive Inhibition as significantly affected EFs can better inform clinical decisions and treatments for AUD. For example, to improve deficient planning and problem-solving skills, treatment could include specific exercises in critical thinking and the development of clearly defined problem-solving techniques as functions mediating the ability to moderate or abstain from alcohol (49–54).

In like manner, distinguishing the affected subcategories of impulsivity can even further refine treatment approaches. Within impulsivity, there is a moderate effect on motor disinhibition, but a large effect on cognitive impulsivity and decisional impulsivity. This finding suggests that although it may be beneficial to concentrate on stimulus control treatment approaches to reduce the effect of motor disinhibition, providing cognitive remediation to ameliorate the damage to the other two aspects of inhibition, cognitive and decisional impulsivity, might be even more effective (54). Much of the literature in substance abuse is currently directed toward the other two facets of impulsivity—impulsive decision-making and the lack of inhibition or inability to prevent a prepotent behavior (55).

Both the decisional and cognitive aspects of impulsivity play a significant role in each phase of the addiction process, including drug acquisition, escalation/dysregulation, and abstinence and relapse (18). Although research has not determined whether these two aspects of impulsivity caused or were caused by alcohol abuse, studies have shown that they predict elevated alcohol consumption and a greater likelihood of relapse (18,56–58). Developing targeted cognitive remediation strategies to reduce these two specific facets of impulsivity could reasonably be expected to curb or disrupt the alcohol addiction process.

The critical importance of EFs in alcohol treatment, especially planning, problem solving, and decisional and cognitive inhibitory abilities, has already prompted the application of promising rehabilitation approaches. For example, Goal Management Training, validated for EF impairments (59), combined with mindfulness-based meditation

(60), produced improved response inhibition and decision-making of outpatients with alcohol abuse problems (61). Continuing research in the precise domains of planning, problem solving, response inhibition, and decision-making could establish additional validated cognitive remediation strategies facilitating improved treatment outcomes.

Limitations and future research

Given the complex and multifactorial nature of EFs, there is no clear consensus for operationalizing terms or agreement on defining component functions, and this study is limited by this ongoing debate. Composites and subcategories of EF are both related and distinct, and so the classifications used in this study could include significantly overlapping features rather than exclusive functions. Likewise, the creation of composites may have the potential to ignore possible and meaningful differences between independent measures within a neuropsychological domain (32). Few studies included in this meta-analysis attempted to distinguish components in EF and impulsivity. Executive tests were apparently selected and interpreted differently depending on the particular research study or clinical neuropsychological orientation. Thus, for the current study, individual tests and measures were assigned to the composites or subcategories based on Testa and colleagues' factors (10), technical data provided by the test developer or primary studies, and long-standing clinical experience with each test in traditional clinical neuropsychological practice (12). This study is thus also limited by this clinical approach in organizing EF test data and not using current experimental models of EF. Since clinical practice varies significantly, future research would benefit from an agreed-upon component structure and inclusion of a broad range of neuropsychological tests targeting all the subcomponents of EFs and impulsivity. Moreover, future meta-analytical research should attempt to test other well-established EF subcomponent models, such as the one developed by Miyake and colleagues (11), in order to provide clinicians and other consumers of neuropsychological data with alternative and potentially better ways to interpret specific tests in relation to their EF domains.

Co-occurring factors are another limitation. Co-occurring disorders are quite high in alcohol abuse, and lower performance on EF tests could also be the result of deficits in other cognitive domains (62). Although there were rigorous attempts to limit the effects from other psychiatric and neurological disorders, given the extensive precursors to alcohol dependence and co-occurrence of psychopathology, other

underlying neuropsychological features may remain that influence the results on the EF tests (63). These premorbid and co-occurring factors should be more reliably and consistently tested and reported in future research. The addition of a comprehensive quality of study assessment, and using it as a moderator would aid in highlighting the association between comorbidities and effect-size in AUD research.

With few studies in this analysis focused exclusively on female populations, and with a lower representation of female subjects throughout most of the other studies, this meta-analysis was limited in its generalizability to women with AUD. Future research should include a balanced distribution between the genders to further examine this important variable.

Conclusion

Given the vast scale of suffering and costs linked to alcohol abuse problems, improved treatment outcomes remain a critical public health concern. Cognitive rehabilitation, especially within the crucial and multifaceted domain of EF, is a promising intervention that could lead to increased treatment compliance and reduced relapse to problematic alcohol consumption. By examining the effect sizes between healthy comparison groups and detoxified subjects with AUD across the five composites of EF and three subcategories of impulsivity, the results of this meta-analysis suggest that Planning & Problem Solving and Inhibition & Self-Regulation—decisional and cognitive impulsivity more than motor disinhibition—are severely affected by alcohol abuse. Cognitive remediation targeting these deficits might increase the related functions mediating the ability to moderate or abstain from alcohol, and so lead to improved treatment results. Future research might aim at establishing the efficacy of such remediation strategies.

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Appendix B: Summary of search strategy and terms for PsycINFO*

The eight searches below are all combined with a Boolean “or” after each is done separately.

Search 1. Precise but broad search using journal names. Searching within every journal that covers the topic of neuropsychology for articles on alcohol dependence or abuse. This search misses all non-neuropsychology journal, but provides a reliable access point to the required information.

(JN = neuropsycholog* or JN = neurocog*) and (DE = (ethanol or alcohol*) or ID = (ethanol or alcohol*))

Search 2. Precise but broad search using all neuropsychology related descriptors selected from the controlled vocabulary list (i.e., The Thesaurus of Psychological Index Terms) combined with the word stems “alcohol* or ethanol*” as descriptors. This search is a descriptor search which will be very precise, but will miss any articles that were published before the terms were introduced into the database and any that were misclassified by the indexing mechanism (whether human or machine).

(DE=(“apraxia” or “ataxia” or “dyskinesia” or “dyspraxia” or “abstraction” or “bender gestalt test” or “benton revised visual retention test” or “body sway testing” or “classification cognitive process” or “cognition” or “cognitive ability” or “cognitive assessment” or “cognitive processes” or “cognitive processing speed” or “cued recall” or “fine motor skill learning” or “finger tapping” or “forgetting” or “free recall” or “halstead reitan neuropsychological battery” or “interference learning” or “kohs block design test” or “learning” or “learning ability” or “long term memory” or “luria nebraska neuropsychological battery” or “matching to sample” or “memory” or “memory disorders” or “memory for designs test” or “motor coordination” or “motor performance” or “motor skills” or “naming” or “neurocognition” or “neuropsychiatry” or “neuropsychological assessment” or “neuropsychology” or “perceptual motor processes” or “prospective memory” or “reaction time” or “retention” or “serial recall” or “spatial ability” or “task switching” or “verbal memory” or “wechsler memory scale” or “wide range achievement test” or “wisconsin card sorting test”) and DE=(alcohol* or ethanol))

Search 3. Precise and narrow search for articles that mention the specific tests combined with alcohol as subject heading (descriptor). This is a test-name search which would miss any article before introducing the capability to search test names in PsycINFO. It also might miss tests that we are not aware of or forgot to include.

(TM=(“american national reading” or “anart” or “Aphasia screening” or “arizona battery” or “Attentional-Blink “ or “auditory verbal learning” or “balloons test” or “bender gestalt” or “Bender Visual-Motor” or “Benton Visual Retention” or “biber figure learning” or “bicycle drawing” or “bisection” or “block construction” or “block counting” or “Block Design” or “BNI” or “boston diagnostic” or “Boston Naming” or “Boston Scanning” or “brief cognitive” or “Brief Visual Memory” or “brief word learning” or “brixton spatial anticipation” or “Bruininks-Oseretsky Test of Motor Proficiency” or “California Verbal Learning” or “camden memory” or “card sorting” or “Category” or “category” or “Category Fluency “ or “cerad” or “closure faces” or “cognistat” or “cognisyst” or “cognitive abilities screening” or “cognitive examination” or “cognitive processing” or “coin

sorting” or “color form sorting” or “Color Span” or “Color-Word Interference” or “complex figure” or “concept formation” or “continuous performance” or “Controlled Oral Word Association” or “Corsi Block” or “Delis-Kaplan Executive Function” or “dementia” or “dichotic listening” or “digit sequence” or “digit span” or “Digit Span Forward” or “Digit Symbol “ or “Digits Backwards” or “discrimination of recency” or “dot counting” or “double memory” or “double simultaneous stimulation” or “draw a person” or “dysexecutive” or “Edinburgh Handedness “ or “everyday memory” or “executive control” or “executive function” or “face recognition” or “face-hand” or “facial recognition” or “famous faces” or “fas” or “figural fluency” or “figure and shape copying” or “finger agnosia” or “finger localization” or “finger oscillation” or “finger recognition” or “Finger Tapping” or “finger tip writing” or “five point test” or “Flicker fusion” or “florida apraxia” or “Forced Recognition” or “Fregly Ataxia Battery” or “frontal assessment battery” or “fuld object-memory” or “General Ability Index” or “graded naming” or “grip strength” or “Grooved Pegboard” or “Halstead” or “heaton figure memory” or “hidden figures” or “hiscock” or “hooper visual organization” or “hopkins verbal learning” or “house drawing” or “incomplete letters” or “Iowa Gambling Task” or “Judgment of Line Orientation” or “kaplan-baycrest” or “kasanin-hanfmann concept formation” or “knox cube” or “learning and memory battery” or “left-right re-orientation” or “letter span” or “line bisection” or “Logical Memory” or “Luria Nebraska” or “Matrix Reasoning” or “maze*” or “memory assessment” or “memory complaints” or “memory control” or “memory for designs” or “memory impairment” or “mental tracking” or “mini-cog” or “minnesota cognitive acuity” or “motor impersistence” or “multilingual aphasia” or “National Adult Reading Test” or “N-Back” or “neurobehavioral cognitive status examination” or “neuropsycholog*” or “neurosensory” or “object assembly” or “Paced Auditory Serial Addition Test” or “paired associate” or “parietal lobe battery” or “pasat” or “peabody” or “peg moving” or “pegboard” or “Perceptual Reasoning” or “personal orientation” or “picture arrangement” or “picture completion” or “Porteus” or “Portland digit” or “presidents test” or “Processing Speed” or “prospective memory” or “proverbs” or “Psychomotor Vigilance” or “random letter test” or “Rapid Automatized Naming” or “repeatable cognitive perceptual” or “Rey Auditory” or “Rey Complex Figure” or “Rey-Osterreith” or “rhythm test” or “right left orientation” or “Rivermead Behavioural Memory” or “ruff figural” or “ruff light trail” or “Seashore Rhythm” or “selective reminding” or “Self-Ordered Pointing” or “sensory-perceptual” or “sentence repetition” or “sentence writing time” or “sequential operations series” or “sequin-goddard formboard” or “Similarities” or “skin writing” or “Speech Sounds Perception “ or “Stroop “ or “Symbol Search” or “tactile finger recognition” or “tactile pattern recognition” or “Tactual Performance” or “tapping” or “test of everyday memory” or “Test of Memory Malinger” or “thurston reasoning” or “thurston word fluency” or “time estimation” or “tinkertoy test” or “token test” or “tower” or “Tower of London” or “Trail Making” or “twenty questions” or “Verbal Comprehension” or “Verbal Paired Associates” or “visual memory span” or “visual naming test” or “visual reproduction” or “visual scanning” or “visual search” or “visual spatial” or “Visual-Search” or “Vocabulary Subtest” or “Wechsler Abbreviated Scale of

Intelligence” or “Wechsler Adult Intelligence Scale” or “Wechsler Memory” or “Wechsler Test of Adult Reading” or “Wide Range Assessment of Memory and Learning” or “Wisconsin Card Sorting” or “woodcock johnson” or “word finding” or “word learning” or “action naming”) and DE= (“alcohol*” or “ethanol”))

Search 4. Less precise but broad search for all test names (see above) we might be interested in. These are to be searched in title, abstract, and other keyword fields (e.g. identifier, descriptor). This search is then combined with alcohol* or ethanol in descriptor and identifier.

Search 5. Imprecise and broad search in title, identifier, and abstract field for the specific names, concepts, and domains of neuropsychological functioning that do not result in excessive false positives. Combine the search with the word stems “alcohol*” or “ethanol*” as either descriptors or in title or identifier. These broad access points should include: memory or “executive function*” or psychomotor or halstead or “verbal learning” or “figure learning”

(TI=(neuropsycholog* or neurocognit* or “cognitive ability” or “language ability” or “language skills” or “verbal fluency” or “verbal ability” or executive? or “novel problem solving” or abstraction or “abstract thinking” or conceptualization or “concept formation” or forgetting or retrieval or “perceptual motor” or psychomotor or “processing speed” or “speed of information processing” or “reaction time” or cerebellar or prefrontal or parietal or ataxia or gait or Halstead or nystagmus or dysdiadochokinesia or dysmetria or dysarthria) or ID=(neuropsycholog* or neurocognit* or “cognitive ability” or “language ability” or “language skills” or “verbal fluency” or “verbal ability” or executive or “novel problem solving” or abstraction or “abstract

thinking” or conceptualization or “concept formation” or forgetting or retrieval or “perceptual motor” or psychomotor or “processing speed” or “speed of information processing” or “reaction time” or cerebellar or prefrontal or parietal or ataxia or gait or Halstead or nystagmus or dysdiadochokinesia or dysmetria or dysarthria) and DE=alcohol*)

Search 6. Imprecise and broad search in only descriptor, title and identifier field for the specific names, concepts, and domains of neuropsychological functioning that would typically result in excessive false positives. Combine the search with the word stems “alcohol*” or “ethanol*” only as descriptor or as identifiers. These broad access points should include:

((DE=(alcohol*) and (DE=(neurolog* or psychomot* or recall or recognition or “prospective memory”) or ID=(neurolog* or psychomot* or recall or recognition or “prospective memory”) or TI=(neurolog* or psychomot* or recall or recognition or “prospective memory”)))

Speech, concentration, memory, learning, motor, and intelligence

Search 7. Precise and broad search using the classification codes 2520 Neuropsychology & Neurology, 2225 Neuropsychological Assessment, and 2226 Health Psychology Testing. The classification codes are then combined with the words “alcohol*” or “ethanol*” in descriptor, identifier or title.

Search 8. Imprecise but broad search using the classification codes 3297 Neurological Disorders & Brain Damage and 2226 Health Psychology Testing. These classification codes are then combined with neuropsycholog* in KW and “alcohol*” or “ethanol*” in descriptor, identifier or title.

*Similar searches were conducted in the other databases, however the controlled vocabulary depended on what is available in the respective database.