



Review article

A meta-analysis of executive dysfunction in patients with schizophrenia: Different degree of impairment in the ecological subdomains of the Behavioural Assessment of the Dysexecutive Syndrome



Maria Lotus Thai^a, Anna Krogh Andreassen^{b,c}, Vibeke Bliksted^{b,c,d,*}

^a OPUS, Outpatient Clinic for Young People with Schizophrenia, Aalborg University Hospital, Psychiatry Department, Brandevej 5, 9220 Aalborg Ø, Denmark

^b Psychosis Research Unit, Aarhus University Hospital Psychiatry, Palle Juul-Jensens Boulevard 99, 8200 Aarhus N, Denmark

^c Department of Clinical Medicine, Aarhus University, Palle Juul-Jensens Boulevard 82, 8200 Aarhus N, Denmark

^d Interacting Minds Centre, Aarhus University, Jens Chr. Skous Vej 4, 8000 Aarhus C, Denmark

ARTICLE INFO

Keywords:

Problem solving
Planning
Cognitive flexibility
Inhibition
Organizing

ABSTRACT

We performed meta-analyses of studies using the 6 subtests of the neuropsychological test battery, the Behavioural Assessment of the Dysexecutive Syndrome (BADS), in order to assess and compare subdomains of executive dysfunction in stable phase patients with schizophrenia relative to healthy controls. The meta-analyses were performed according to the PRISMA statement. A systematic literature search was performed yielding 10 studies for inclusion ($N_{SCH} = 375$; $N_{HC} = 541$). Meta-analyses were done using Stata IC 14. Due to large heterogeneity and the few number of studies a random-effects model was used along with Hedges' g . Results showed that relative to healthy controls, patients with schizophrenia overall performed significantly worse in all subtests of BADS. However, moderate effect sizes were seen with regard to temporal estimation and strategy-forming, while very large effect sizes were seen regarding complex forward planning, inhibition, cognitive flexibility and novel problem solving. The findings from this meta-analysis demonstrate a significant difference between patients with (primarily) longer lasting schizophrenia and healthy control subjects on all subdomains of executive functions (EF). But some aspects of EF seem to be more severely affected than others. Future research and clinical interventions need to differentiate between subdomains of EF.

1. Introduction

A considerable amount of empirical research has attempted to chart the area of neurocognitive functioning in schizophrenia (SZ). Several meta-analyses and systematic reviews (Bowie et al., 2006; Harvey et al., 2005; Heinrichs and Zakzanis, 1998; Mesholam-Gately et al., 2009; Reichenberg and Harvey, 2007) consistently show that moderate to severe impairments characterize patients with SZ across the seven cognitive domains included in the MATRICS Consensus Cognitive Battery such as IQ, attention, learning, visual and verbal memory, language, and executive function (Fatouros-Bergman et al., 2014; Fioravanti et al., 2012; Fioravanti et al., 2005; Nuechterlein et al., 2008). It is a robust finding that executive dysfunction represents one of the most frequent and manifest neurocognitive impairments in schizophrenia (Fatouros-Bergman et al., 2014; Heinrichs and Zakzanis, 1998; Johnson-Selfridge and Zalewski, 2001; Raffard and Bayard, 2012; Reichenberg and Harvey, 2007; Aas et al., 2014). Cognitive neuroscience has provided models that explain some of the component

mechanisms of the executive deficits in patients with schizophrenia, e.g. rule generation and selection, and dynamic adjustments in control (Kerns et al., 2008). Processing of rules involves: the dorsolateral regions of the prefrontal cortex (DLPFC) (sustaining maintenance of goal or rule information), subcortical systems in the basal ganglia (contributing to selective rule updating by "Go" and "NoGo" neurons), and neurotransmitters involved in a gate mechanism in the DLPFC such as dopamine D1 receptors (involved in closing the gate and securing stable maintenance), and dopamine D2 receptors (involved in rapid updating). Furthermore, norepinephrine is involved in interference control mechanisms in PFC, and norepinephrine and N-methyl d-aspartate receptors are thought to be of significant importance in rule selection (Kerns et al., 2008). The ability to adjust behaviour and cognition simultaneously based on an ongoing performance is referred to as dynamic adjustments in control. This process involves the dorsal anterior cingulate cortex (ACC) (performance monitoring) in close interaction with other brain areas such as DLPFC, basal ganglia, and the locus coeruleus by dopaminergic input contributing to various processes of

* Corresponding author at: Palle Juul-Jensens Boulevard 99, Indgang K, Plan 5, K510-104, DK-8200 Aarhus N, Denmark.

E-mail address: vibeke.bliksted@ps.rm.dk (V. Bliksted).

<https://doi.org/10.1016/j.psychres.2018.12.088>

Received 5 April 2018; Received in revised form 14 December 2018

Available online 20 December 2018

0165-1781/ © 2018 Elsevier B.V. All rights reserved.

error monitoring (Kerns et al., 2008). Studies have found reduced DLPFC gray matter volume in patients with schizophrenia dominated by comprehensive deficit in executive functions (Orellana and Slachevsky, 2013). Furthermore, it has been shown that patients with schizophrenia have altered neural activity in the DLPFC, ACC and the mediodorsal nucleus of the thalamus, while at the same time showing increased activity in other areas of the PFC, which might be due to compensatory mechanisms (Orellana and Slachevsky, 2013). Finally, neuroimaging has revealed abnormal connectivity in the three fronto-cortical circuits that are involved in cognitive and behavioural control (the DLPFC, orbitofrontal cortex (OFC), and ACC) in patients with schizophrenia (Orellana and Slachevsky, 2013). The EF deficits seen in patients with schizophrenia could be seen as part of the overall neurodevelopmental hypothesis suggesting that interactions between environmental and genetic factors during critical stages of early brain development underlies later development of schizophrenia (Fatemi and Folsom, 2009).

The definition of the term executive functions (EF) lacks consensus. In addition, several researchers agree that a common theoretical ground for the construct is missing (Barkley, 2012; Jurado and Rosselli, 2007; Savla et al., 2010). In spite of this lack of consent, the concept of EF is often described as an umbrella term covering a diverse set of cognitive capacities to guide, monitor, and control our actions and mental processes to meet particular goals in a purposeful manner. Executive functions (EF) may be defined as higher-order neurocognitive functions consisting of abilities to plan and structure goal-directed activity and problem-solving behaviour in a strategic, flexible manner or as merely the ability to respond in an adaptive way to novel situations (Chan et al., 2008; Diamond, 2013; Jacques and Marcovitch, 2010; Jurado and Rosselli, 2007; Katz et al., 2007). These complex cognitive processes are crucial for many aspects of daily functioning, and thus, executive dysfunction has a significant impact on academic, vocational, emotional, social, and adaptive functioning (Bowie et al., 2006; Hunter and Sparrow, 2012; Jacques and Marcovitch, 2010; Jurado and Rosselli, 2007). This warrants for enhancement of domain-specific interventions like cognitive remediation or rehabilitation targeted at EF in order to improve the level of functioning in schizophrenia (Kluwe-Schiavon et al., 2013).

A strong branch of the theoretical field views EF as an independent domain covering a set of related cognitive control processes. Within this branch, the ‘fractionation approach’ to EF deficits presumes that EF consist of various subcomponents (e.g., cognitive flexibility, inhibition, planning, and problem solving) that may be heterogeneously impaired in the individual (Chan et al., 2006a,b; Raffard and Bayard, 2012). The lack of agreement concerning theoretical positions and operationalisations of the construct has clearly affected the assessment area of EF that is dominated by the psychometric approach. This approach uses a wide variety of neuropsychological tasks claiming to measure different cognitive processes associated with behaviour presumably demanding intact executive functioning (Barkley, 2012). In the wake of this divergence, critical issues arise concerning task impurity, task simplification, and ecological validity among other methodological issues, which must be considered in a research as well as a clinical context in order to reinforce the field of neuropsychological assessment of EF in schizophrenia (Barkley, 2012; Burgess et al., 1998; Hunter and Sparrow, 2012).

Many neuropsychological tests are only moderately correlated to everyday functioning (Chaytor and Schmitter-Edgecombe, 2003). Problems with the ecological test validity is further challenged in patients with schizophrenia, where psychotic symptoms (e.g. auditory hallucinations and formal thought disorder) and negative symptoms (e.g. physical anergia and imperistence) may interfere with test performance. Furthermore, the comprehensive cognitive deficits in these patients may cause more basic cognitive deficits (such as attention) to interfere with the results of more complex cognitive functions (such as EF). Attempting to address the problems of inadequate ecological

validity and task simplification regarding EF assessment, a British research group developed a test battery, ‘The Behavioural Assessment of the Dysexecutive Syndrome (BADS)’ with the aim of measuring EF impairment with tasks resembling everyday life activities requiring EF (Evans et al., 1997; Norris and Tate, 2000; Wilson et al., 1997,1998). According to this research group, an advantage of BADS is that it consists of six subtests tapping several different aspects of EF (Wilson et al., 1998) which is consistent with the fractionation approach to executive dysfunction (Raffard and Bayard, 2012). The BADS was originally developed to detect executive dysfunction in patients with traumatic brain-injuries and other neurological disorders (Wilson et al., 1998). However, the initial studies compared brain-injured samples to both patients with longer lasting SZ and healthy controls. In both studies, the patient groups were significantly impaired on most subtests of BADS relative to healthy controls, but the differences between patients with SZ and the patients with brain-injuries were non-significant (Evans et al., 1997; Wilson et al., 1998). Only Wilson et al. (1998) found a significant difference between patient groups on a subtest of BADS, i.e., Zoo Map. Moreover, the only non-significant difference between patients with longer lasting SZ and controls was found on Temporal Judgment.

So far, no publication has attempted to complete a systematic overview of findings from studies using subtests of BADS to assess executive dysfunction in schizophrenia. This meta-analysis was performed in order to make a statistical summarization of studies that compare the performance of patients with SZ and healthy controls using BADS. By producing separate meta-analyses of each BADS subtest, we aim to shed further light on whether SZ is better characterized by a general executive dysfunction or by deficits in specific EF components. The BADS was chosen among other ecological EF tests since it is translated into several languages and can be performed as part of traditional neuropsychological testing.

2. Methods and materials

2.1. Executive test battery

‘The Behavioural Assessment of Dysexecutive Syndrome (BADS)’ consists of six subtests claimed to measure different EF components. *Rule Shift Cards* (i.e., cognitive flexibility/set shifting, inhibition) requires the subject to shift from one rule to another when viewing a deck of playing cards. In *Action Program* (i.e., novel problem solving, planning), the subject must remove a cork from the bottom of a glass tube by using a set of unfamiliar tools while keeping certain rules in mind. In *Key Search* (i.e., planning, monitoring own performance), the subject must draw a path inside a square resembling a field to show, how he would search the field to find his lost keys. *Temporal Judgment* (i.e., estimation of time) consists of four questions of time estimation. In *Zoo Map* (i.e., planning a route, inhibition), the subject is asked to plan and draw a route through a zoo while keeping various rules in mind. Finally, the *Modified Six Elements Test (MSET)* (i.e., planning, problem solving, organization, inhibition) examines the subject's ability to structure his performance of a set of tasks within ten minutes in accordance with certain rules. For each subtest, a summary profile score can be obtained with a minimum of zero and a maximum of four. In addition, these six profile scores can be added up to a total profile score ranging from 0 to 24

2.2. Procedures

This meta-analysis was performed according to the Preferred Reporting Items for a Systematic Review and Meta-analysis, the PRISMA statement (Stewart et al., 2015). The PICO question of this meta-analysis was: Population: The study must include an experimental group of adult patients with schizophrenia in a stable phase of illness (mean age > 18 but < 65 years old) diagnosed according to

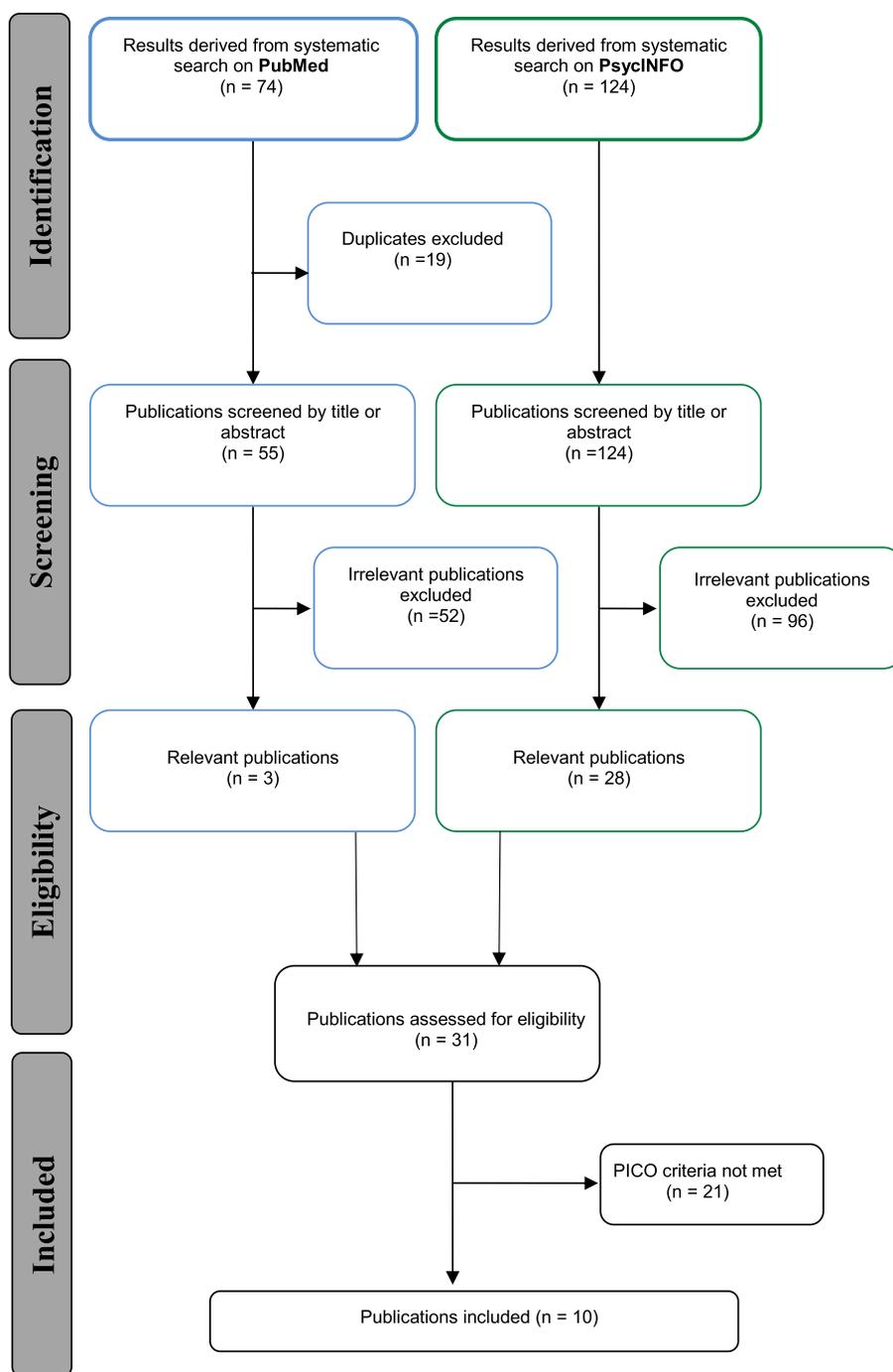


Fig. 1. PRISMA flow chart illustrating the search strategy and the inclusion/exclusion criteria.

contemporary diagnostic criteria (DSM-III (APA) or later; International Classification of Diseases, Ninth Revision (ICD-9) or later; Research Diagnostic Criteria – RDC) (Spitzer et al., 1978). Intervention: The study must include (but not necessarily report) all standardized subtest and measures of BADS (Rule Shift Cards, Action Program, Key Search, Temporal Judgment, Zoo Map, Modified Six Elements Test, and Total Profile Score). Comparison: The study must include a matched healthy comparison group. Outcome: The study must report results in terms of means and standard deviations on the BADS' subtests for the experimental group and the comparison group. Furthermore, the following exclusion criteria were used: a) the paper did not include an experimental study (e.g., an unsystematic review); b) the paper reported data on an experimental group with more than 15% of the sample being patients with other diagnoses than schizophrenia (e.g., schizoaffective

or schizophreniform disorder, affective psychosis, psychosis not-otherwise-specified).

2.3. Data sources and search strategy

Using two electronic databases, PsycINFO and PubMed, a systematic free text search was performed independently by MLT and AKA the 1st of September 2017 in order to detect studies of relevance. For inclusion, studies had to be a) peer reviewed, b) published after 1995, and c) journal articles published in an English language journal. The following combinations of keywords were utilized: *schizophrenia AND BADS OR Behavioural Assessment of Dysexecutive Syndrome*.

2.4. Meta-analyses

Statistical meta-analyses were performed with Stata IC 14 software for Windows (Palmer and Sterne, 2016). Effect sizes were calculated based on means and standard deviations for each between-group comparison on the six BADS subtests scores as well as on the BADS Total Profile Score. Chi-squared tests (χ^2) were used to test the heterogeneity of the resulting mean-weighted effect sizes. I^2 -tests were used to measure percentage of variation across studies in standardized mean difference (SMD) attributable to heterogeneity. A value of 0.25% corresponds to low, 0.50% to moderate, and 0.75% to high heterogeneity. Due to the small number of studies implemented in the meta-analyses, effect sizes were estimated using Hedges' g ³⁰. In Hedges' methods, the differences in means are divided by an estimate of the standard deviation. Moreover, a small sample bias correction factor is incorporated in the calculations of Hedges' g . Random-effects models as well as Hedges' g were used for the meta-analysis due to large heterogeneity. Tau^2 -tests were used in the meta-analysis with random-effects models to find an estimate of between-study variances. Due to the small number of studies available, it was not possible to check for publication bias.

3. Results

3.1. Selection process and data extraction

Following a four-step procedure, the publications were evaluated for inclusion. During the first step, the following combination of keywords were utilized: PsycINFO: *schizophrenia* AND *BADS* OR *Behavioural Assessment of Dysexecutive Syndrome* (124 articles). PubMed: *schizophrenia* AND *BADS* OR *Behavioural Assessment of Dysexecutive Syndrome* (74 articles). This search identified 198 publications including duplicates. During the second step, 179 studies were screened based on a title and abstract in order to eliminate studies that obviously failed to meet the inclusion criteria. 31 studies were examined in detail concerning eligibility. 12 studies were excluded due to lack of control group, 6 studies did not use the BADS battery, one study used diagnoses from a medical chart, one study did not provide means and SD's of the BADS battery, one paper was not available online (see supplementary material). Finally, 10 publications were included in this meta-analysis (see details in Fig. 1 Flow chart).

3.2. BADS subtests and total score

Table 1 shows N , mean and SD of the included studies. Overall, data from 375 patients with schizophrenia and 541 matched healthy controls were included in the meta-analyses. Four studies only reported total scores (Amann et al., 2012; Knolle-Veentjer et al., 2008; Krabbendam et al., 1999; Peters et al., 2007). Authors were contacted but we were not able to get further data. This meant that meta-analyses of all the BADS subtest were done with $N = 254$ patients with schizophrenia and $N = 416$ healthy controls (Evans et al., 1997; Katz et al., 2007; Silva et al., 2014; Tyson et al., 2008; Vargas et al., 2009; Wilson et al., 1998).

The standardized mean differences (SMD) between patients with SZ and controls on the six BADS subtests as well as the BADS Total Profile score are reported in Table 2. Forest plots of the subtests can be seen in the Supplementary material (S1-S6). All reported differences between SZ and HC were significant, and effect sizes were moderate to large indicating that patients with SZ were significantly impaired in the EF domains measured with BADS relative to healthy controls. The largest overall effect size was found on BADS Total Profile score, SMD -1.70 95% CI(-2.17 ; -1.24), and the smallest effect sizes was found on BADS Temporal Judgment, SMD = -0.76 95% CI(-1.18 ; -0.34) and Key Search, SMD = -0.85 95% CI(-1.17 ; -0.55). The largest effect sizes for individual subtests were found on Modified Six Elements,

Table 1
Characteristics and BADS test scores of the included studies.

Study(year)	N_{SZ}/N_{HC}	Rule shift cards M(SD)	Action program M(SD)	Key search M(SD)	Temporal judgement M(SD)	Zoo map M(SD)	Modified six elements M(SD)	Total profile score M(SD)
Amann et al. (2012)	45/65	N/A	N/A	N/A	N/A	N/A	N/A	SCH: 73.78(19.81) HC: 96.58(13.11)
Evans et al. (1997)	31/26	SCH: 2.94(1.29) HC: 3.62(1.75)	SCH: 2.73(1.34) HC: 3.89(0.33)	SCH: 1.83(1.23) HC: 3.00(1.33)	SCH: 1.84(1.13) HC: 2.50(0.65)	SCH: 1.00(1.41) HC: 1.72(1.49)	SCH: 2.27(1.20) HC: 3.52(0.79)	SCH: 12.79(4.58) HC: 18.00(2.95)
Katz et al. (2007)	31/93	SCH: 1.42(1.23) HC: 3.47(0.919)	SCH: 1.90(1.37) HC: 3.58(0.94)	SCH: 1.26(1.13) HC: 2.58(1.21)	SCH: 1.26(0.82) HC: 1.79(0.90)	SCH: 0.52(0.81) HC: 2.54(1.14)	SCH: 1.77(0.80) HC: 3.46(0.82)	SCH: 8.13(3.91) HC: 17.41(3.16)
Knolle-Veentjer et al. (2008)	29/23	N/A	N/A	N/A	N/A	N/A	N/A	SCH: 87.83(19.13) HC: 110.60(12.19)
Krabbendam et al. (1999)	24/17	N/A	N/A	N/A	N/A	N/A	N/A	SCH: 16.10(3.80) HC: 19.10(2.20)
Peters et al. (2007)	23/20	N/A	N/A	N/A	N/A	N/A	N/A	SCH: 14.04(4.01) HC: 20.05(2.04)
Silva et al. (2014)	65/31	SCH: 2.18(1.17) HC: 3.81(0.40)	SCH: 2.41(1.18) HC: 3.52(0.57)	SCH: 1.15(1.08) HC: 2.68(1.14)	SCH: 1.38(0.74) HC: 2.81(0.85)	SCH: 1.26(0.86) HC: 3.74(0.45)	SCH: 2.15(0.66) HC: 3.97(0.18)	SCH: 10.65(3.07) HC: 20.55(1.79)
Tyson et al. (2008)	36/15	SCH: 3.20(0.80) HC: 3.70(0.50)	SCH: 3.40(1.00) HC: 3.90(0.50)	SCH: 2.30(1.20) HC: 2.60(1.20)	SCH: 1.90(0.90) HC: 2.40(1.10)	SCH: 1.60(1.10) HC: 1.90(1.20)	SCH: 3.00(1.10) HC: 3.50(0.80)	SCH: 15.40(3.40) HC: 18.00(2.40)
Vargas et al. (2009)	60/35	SCH: 2.50(1.37) HC: 3.66(0.76)	SCH: 2.93(1.12) HC: 3.80(0.47)	SCH: 1.57(1.39) HC: 2.74(1.29)	SCH: 1.50(0.91) HC: 2.09(1.07)	SCH: 1.48(1.16) HC: 2.80(1.18)	SCH: 2.47(1.18) HC: 3.29(0.86)	SCH: 12.43(4.30) HC: 18.37(2.88)
Wilson et al. (1998)	31/216	SCH: 2.94(1.29) HC: 3.56(0.87)	SCH: 2.73(1.34) HC: 3.77(0.52)	SCH: 1.88(1.23) HC: 2.60(1.32)	SCH: 1.84(1.13) HC: 2.15(0.91)	SCH: 1.00(1.41) HC: 2.44(1.13)	SCH: 2.27(1.20) HC: 3.52(0.80)	SCH: 12.79(4.58) HC: 18.05(3.05)

Table 2
Tests and effect sizes (Hedges' g) for the meta-analyses of BADS subtests. Due to large heterogeneity and few number studies (<10) a random-effects model was used together with Hedges' g.

BADS score	N_{SCH} / N_{HC}	SMD (95%CI)	Heterogeneity	Variation in SMD attributable to heterogeneity	Estimate of between-study variance	Test of SMD = 0
Rule shift cards	254/416	-1.08(-1.57; -0.58)	$\chi^2(5) = 32.23$ $P < 0.001$	$I^2 = 84.5\%$	$Tau^2 = 0.32$	$Z = 4.24$ $P < 0.001$
Action program	254/416	-1.16(-1.46; -0.87)	$\chi^2(5) = 11.42$ $P = 0.04$	$I^2 = 56.2\%$	$Tau^2 = 0.08$	$Z = 7.72$ $P < 0.001$
Key search	254/416	-0.85(-1.17; -0.55)	$\chi^2(5) = 12.46$ $P = 0.03$	$I^2 = 59.9\%$	$Tau^2 = 0.08$	$Z = 5.54$ $P < 0.001$
Temporal judgement	254/416	-0.76(-1.18; -0.34)	$\chi^2(5) = 24.26$ $P < 0.001$	$I^2 = 79.4\%$	$Tau^2 = 0.22$	$Z = 3.52$ $P < 0.001$
Zoo map	254/416	-1.37(-2.01; -0.64)	$\chi^2(5) = 63.38$ $P < 0.001$	$I^2 = 92.1\%$	$Tau^2 = 0.75$	$Z = 3.69$ $P < 0.001$
Modified six elements test	254/416	-1.52(-2.23; -0.82)	$\chi^2(5) = 57.60$ $P < 0.001$	$I^2 = 91.3\%$	$Tau^2 = 0.70$	$Z = 4.26$ $P < 0.001$
Total profile score	375/541	-1.70(-2.17; -1.24)	$\chi^2(9) = 64.15$ $P < 0.001$	$I^2 = 86.0\%$	$Tau^2 = 0.47$	$Z = 7.21$ $P < 0.001$

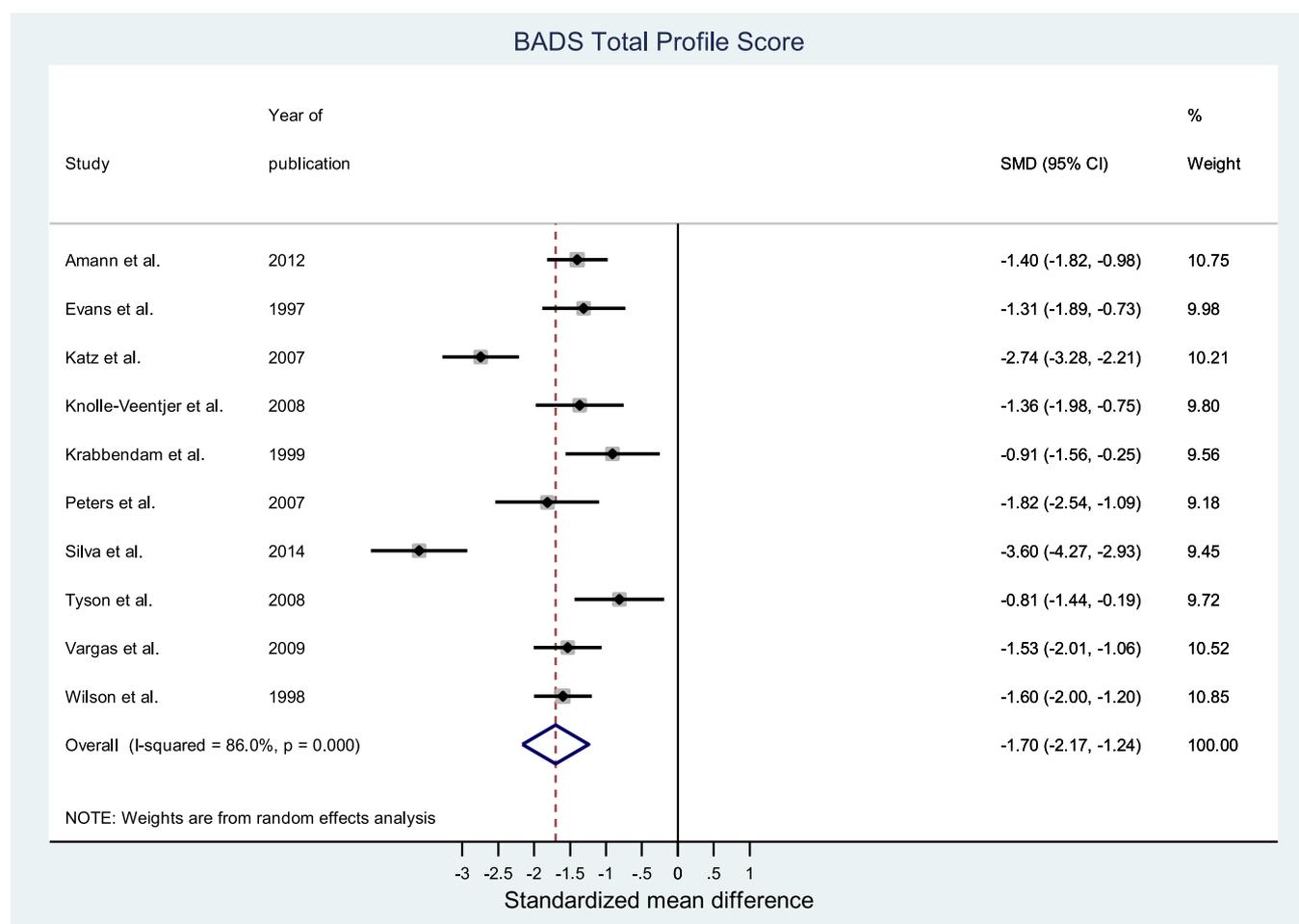


Fig. 2. Forest plot of BADS total profile score.

SMD = -1.52 95% CI(-2.23; -0.82) and Zoo Map, SMD = -1.37 95% CI(-2.01; -0.64) (Fig. 2).

4. Discussion

The present meta-analysis was performed with the purpose of statistically summarizing the performance of patients with schizophrenia compared to matched healthy control groups on subtests of a comprehensive test battery, ‘The Behavioural Assessment of the Dysexecutive Syndrome’ (BADS) reflecting everyday executive functions. The results

provide evidence of significant differences between patients with SZ and healthy controls in performance on all BADS subtests including BADS Total Profile Score, which showed the largest effect size, SMD = -1.70 95%CI (-2.17; -1.24). Four out of six individual subtests revealed a large SMD value (Action Program, MSET, Zoo Map and Rule Shift Cards) with SZ performed one standard deviation or more below the controls indicating large EF impairments. These subtests represent complex executive subdomains such as the ability to inhibit pre-learned behavior, organizing and planning, novel problem solving and forward planning. Two subtests showed effect sizes below

one SMD with a moderate effect size (Temporal Judgment and Key Search). These tests reflect more simple aspects of EF such as strategy-forming and estimation of time. Thus, patients with SZ may experience smaller impairments in less complicated aspects of EF. Overall, results shows that the patients with SZ included in the meta-analysis suffered from moderate to large impairments in the specific EF components measured with BADS. As patients with SZ performed significantly worse on all subtests of BADS compared to healthy controls, this clinical group seems to present with a general impairment of EF. However, one cannot neglect that in two subtests, this patient group only showed moderate impairment. This indicates that not all components of EF may be equally impaired in patients with SZ. Thus, the results support the fractionation approach to EF deficits in schizophrenia (Chan et al., 2006a,b,2008; Raffard and Bayard, 2012).

It is important to bear in mind that BADS in full may not be the perfect instrument to assess executive dysfunction after all. Although the six subtests of BADS cover a broad range of everyday EF components, they do not assess all aspects of executive functioning. Some may claim that measures of working memory aspects are missing while measures of spatial planning abilities are overrepresented. Besides, as in many other neuropsychological EF tasks there are a considerable overlap between the EF components measured within the individual subtests. Furthermore, the level of complexity afforded to solve some of the problems in BADS efficiently may be too low compared to other EF tasks. For instance, Rule Shift Cards is a set shifting task with only one shift between two rules and thus, has a very low complexity level compared to the traditionally used WCST (Wisconsin Card Sorting Test) (Puente, 1985), which includes several shifts per trial. The limitations of the assessment instrument in question have direct implications for the interpretation of our results. Even though the meta-analysis shows that patients with SZ experience dysfunction in several EF components measured with BADS, this may not be generalizable to all potential aspects of EF. It is also difficult to answer the question of which exact EF components are affected in schizophrenia, as most BADS subtests measure more than one aspect of EF, which makes interpretation of test results ambiguous. However, the fact that even BADS tasks with low levels of complexity still result in poor performance for patients with SZ means that our findings of large EF impairments in schizophrenia are relatively robust.

However, the meta-analysis has several limitations. First, the relative small number of studies included may have a significant impact on results. Second, we performed no meta-analytic regression analysis controlling for moderator variables such as medication, symptom level, duration of illness, age, gender, education, or general cognition. Third, a few studies in the meta-analysis did not use the recommended scoring system for BADS subtest profile scores ranging from 0–4. These differences in the scoring approach complicate the comparison of results. Fourth, a majority of the studies examined a patient sample with longer lasting schizophrenia. Thus, the results are not necessarily generalizable to patients with first-episode schizophrenia. Still, a relative strength of the meta-analysis is that we only included studies with patient samples consisting of more than 75% patients with a diagnosis of schizophrenia and excluded all other psychotic disorders in the schizophrenia spectrum, which resulted in a ‘pure’ schizophrenia sample.

Within the area of neurocognitive functioning in schizophrenia, more studies are needed that focus specifically on executive dysfunction. These studies must include a number of relevant EF tasks covering a broad range of EF components such as working memory, cognitive flexibility, planning, and problem solving. Longitudinal studies are also warranted that investigate the relationship between schizophrenia and executive dysfunction over time. In order to find out whether executive dysfunction is characteristic in different schizophrenia subgroups, future studies should compare the performance of patients with first-episode schizophrenia to patients with longer lasting schizophrenia on BADS as well as other EF tasks while controlling for impairment in other cognitive domains, symptom level, duration of illness etc. Finally,

an interesting line of research would be to study the relationship between functional outcome (e.g., vocational, social, and community functioning) and executive dysfunction in various schizophrenia subgroups such as patients with first-episode schizophrenia and patients with longer lasting schizophrenia.

Conflict of interest

None.

Contributors

MLT and AKA did the two independent literature searches. MLT and AKA did the data extraction. MLT, AKA and VB did the tables with summary of findings. VB did the meta-analyses. MLT made the first draft of the paper. AKA and VB finalized the paper.

References

- Amann, B., Gomar, J., Ortiz-Gil, J., McKenna, P., Sans-Sansa, B., Sarro, S., et al., 2012. Executive dysfunction and memory impairment in schizoaffective disorder: a comparison with bipolar disorder, schizophrenia and healthy controls. *Psychol. Med.* 42 (10), 2127–2135.
- Barkley, R.A., 2012. *Executive Functions: What they are, How They Work, and Why they Evolved*. Guilford Press, New York.
- Bowie, C.R., Reichenberg, A., Patterson, T.L., Heaton, R.K., Harvey, P.D., 2006. Determinants of real-world functional performance in schizophrenia subjects: correlations with cognition, functional capacity, and symptoms. *Am. J. Psych.* 163 (3), 418–425.
- Burgess, P.W., Alderman, N., Evans, J., Emslie, H., Wilson, B.A., 1998. The ecological validity of tests of executive function. *J. Int. Neuropsychol. Soc.* 4 (6), 547–558.
- Chan, R.C., Chen, E.Y., Cheung, E.F., Chen, R.Y., Cheung, H., 2006a. The components of executive functioning in a cohort of patients with chronic schizophrenia: a multiple single-case study design. *Sch. Res.* 81 (2), 173–189.
- Chan, R.C., Chen, E.Y., Law, C., 2006b. Specific executive dysfunction in patients with first-episode medication-naïve schizophrenia. *Sch. Res.* 82 (1), 51–64.
- Chan, R.C., Shum, D., Touloupoulou, T., Chen, E.Y., 2008. Assessment of executive functions: review of instruments and identification of critical issues. *Arc. Clin. Neuropsychol.* 23 (2), 201–216.
- Chaytor, N., Schmitter-Edgecombe, M., 2003. The ecological validity of neuropsychological tests: a review of the literature on everyday cognitive skills. *Neuropsychol. Rev.* 13 (4), 181–197.
- Diamond, A., 2013. Executive functions. *Annu. Rev. Psychol.* 64, 135–168.
- Evans, J., Chua, S., McKenna, P., Wilson, B., 1997. Assessment of the dysexecutive syndrome in schizophrenia. *Psychol. Med.* 27 (3), 635–646.
- Fatemi, S.H., Folsom, T.D., 2009. The neurodevelopmental hypothesis of schizophrenia, revisited. *Sch. Bull.* 35 (3), 528–548.
- Fatouros-Bergman, H., Cervenka, S., Flyckt, L., Edman, G., Farde, L., 2014. Meta-analysis of cognitive performance in drug-naïve patients with schizophrenia. *Sch. Res.* 158 (1), 156–162.
- Fioravanti, M., Bianchi, V., Cinti, M.E., 2012. Cognitive deficits in schizophrenia: an updated metanalysis of the scientific evidence. *BMC Psych.* 12 (1), 64.
- Fioravanti, M., Carlone, O., Vitale, B., Cinti, M.E., Clare, L., 2005. A meta-analysis of cognitive deficits in adults with a diagnosis of schizophrenia. *Neuropsychol. Rev.* 15 (2), 73–95.
- Harvey, P.D., Koren, D., Reichenberg, A., Bowie, C.R., 2005. Negative symptoms and cognitive deficits: what is the nature of their relationship? *Sch. Bull.* 32 (2), 250–258.
- Heinrichs, R.W., Zakzanis, K.K., 1998. Neurocognitive deficit in schizophrenia: a quantitative review of the evidence. *Neuropsychology* 12 (3), 426.
- Hunter, S.J., Sparrow, E.P., 2012. *Executive Function and dysfunction: Identification, Assessment and Treatment*. Cambridge University Press, Cambridge.
- Jacques, S., Marcovitch, S., 2010. Development of executive function across the life span. In: Lerner, R.M., Willis, F.O. (Eds.), *The Handbook of Life-span Development*. John Wiley and Sons Ltd., Chichester, United Kingdom.
- Johnson-Selfridge, M., Zalewski, C., 2001. Moderator variables of executive functioning in schizophrenia: meta-analytic findings. *Sch. Bull.* 27 (2), 305–316.
- Jurado, M.B., Rosselli, M., 2007. The elusive nature of executive functions: a review of our current understanding. *Neuropsychol. Rev.* 17 (3), 213–233.
- Katz, N., Tadmor, I., Felzen, B., Hartman-Maeir, A., 2007. Validity of the executive function performance test in individuals with schizophrenia. *OTJR* 27 (2), 44–51.
- Kerns, J.G., Nuechterlein, K.H., Braver, T.S., Barch, D.M., 2008. Executive functioning component mechanisms and schizophrenia. *Biol. Psych.* 64 (1), 26–33.
- Kluwe-Schiavon, B., Sanvicente-Vieira, B., Kristensen, C., Grassi-Oliveira, R., 2013. Executive functions rehabilitation for schizophrenia: a critical systematic review. *J. Psychiatr. Res.* 47 (1), 91–104.
- Knolle-Veentjer, S., Huith, V., Ferstl, R., Aldenhoff, J.B., Hinze-Selch, D., 2008. Delay of gratification and executive performance in individuals with schizophrenia: putative role for eating behavior and body weight regulation. *J. Psychiatr. Res.* 42 (2), 98–105.
- Krabbendam, L., de Vugt, M.E., Derix, M.M., Jolles, J., 1999. The behavioural assessment

- of the dysexecutive syndrome as a tool to assess executive functions in schizophrenia. *Clin. Neuropsychol.* 13 (3), 370–375.
- Mesholam-Gately, R.I., Giuliano, A.J., Goff, K.P., Faraone, S.V., Seidman, L.J., 2009. Neurocognition in first-episode schizophrenia: a meta-analytic review. *Am. Psychol. Ass.*
- Norris, G., Tate, R.L., 2000. The behavioural assessment of the dysexecutive syndrome (BADS): ecological, concurrent and construct validity. *Neuropsychol. Rehab.* 10 (1), 33–45.
- Nuechterlein, K.H., Green, M.F., Kern, R.S., Baade, L.E., Barch, D.M., Cohen, J.D., et al., 2008. The MATRICS consensus cognitive battery, part 1: test selection, reliability, and validity. *Am. J. Psych.* 165 (2), 203–213.
- Orellana, G., Slachevsky, A., 2013. Executive functioning in schizophrenia. *Front Psychiatry* 4, 35.
- Palmer, T., Sterne, J.A., 2016. Meta-analysis in Stata: an Updated Collection from the Stata Journal. Stata Press, New York.
- Peters, M.J., Cima, M.J., Smeets, T., de Vos, M., Jelicic, M., Merckelbach, H., 2007. Did I say that word or did you? Executive dysfunctions in schizophrenic patients affect memory efficiency, but not source attributions. *Cogn. Neuropsych.* 12 (5), 391–411.
- Puente, A., 1985. Wisconsin card sorting test. *Test Crit.* 4, 677–682.
- Raffard, S., Bayard, S., 2012. Understanding the executive functioning heterogeneity in schizophrenia. *Brain Cogn.* 79 (1), 60–69.
- Reichenberg, A., Harvey, P.D., 2007. Neuropsychological impairments in schizophrenia: Integration of performance-based and brain imaging findings. *Psychol. Bull.* 133 (5), 833.
- Savla, G.N., Twamley, E.W., Delis, D.C., Roesch, S.C., Jeste, D.V., Palmer, B.W., 2010. Dimensions of executive functioning in schizophrenia and their relationship with processing speed. *Sch. Bull.* 38 (4), 760–768.
- Silva, T., Monteiro, L., Lopes, E., 2014. INECO frontal screening: an instrument to assess executive dysfunction in schizophrenia. *Span. J. Psychol.* 17.
- Spitzer, R.L., Endicott, J., Robins, E., 1978. Research diagnostic criteria: rationale and reliability. *Arch. Gen. Psych.* 35 (6), 773–782.
- Stewart, L.A., Clarke, M., Rovers, M., Riley, R.D., Simmonds, M., Stewart, G., et al., 2015. Preferred reporting items for a systematic review and meta-analysis of individual participant data: the PRISMA-IPD statement. *JAMA* 313 (16), 1657–1665.
- Tyson, P.J., Laws, K.R., Flowers, K.A., Mortimer, A.M., Schulz, J., 2008. Attention and executive function in people with schizophrenia: Relationship with social skills and quality of life. *Int. J. Psych. Clin. Pract.* 12 (2), 112–119.
- Vargas, M.L., Sanz, J.C., Marín, J.J., 2009. Behavioral assessment of the dysexecutive syndrome battery (BADS) in schizophrenia: a pilot study in the Spanish population. *Cogn. Behav. Neurol.* 22 (2), 95–100.
- Wilson, B.A., Evans, J.J., Alderman, N., Burgess, P.W., Emslie, H., 1997. Behavioural assessment of the dysexecutive syndrome. In: Rabbitt, P. (Ed.), *Methodology of Frontal and Executive Function*. Psychology Press, Hove, United Kingdom, pp. 239–250.
- Wilson, B.A., Evans, J.J., Emslie, H., Alderman, N., Burgess, P., 1998. The development of an ecologically valid test for assessing patients with a dysexecutive syndrome. *Neuropsychol. Rehab.* 8 (3), 213–228.
- Aas, M., Dazzan, P., Mondelli, V., Melle, I., Murray, R.M., Pariante, C.M., 2014. A systematic review of cognitive function in first-episode psychosis, including a discussion on childhood trauma, stress, and inflammation. *Front Psychiatry*, 4, 182.