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Review Article

Impaired set-shifting ability in patients with bulimia nervosa: A systematic review and meta-analysis

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Abstract

Introduction: Previous research has shown that there is a link between bulimia nervosa (BN) diagnosis and set-shifting disability although with some conflicting results, yet no meta-analyses have examined the BN pathology with set-shifting. The aim of the present research is to critically appraise and synthesize the literature relating to set-shifting ability in Bulimia Nervosa.

Materials and Methods: Four databases (PubMed, PsycINFO, Scopus, and Google Scholar) were searched for eligible studies. The 8 selected studies contained (with 24 effect sizes) both bulimia nervosa disorder and healthy control groups, and employed at least one of the following six neuropsychological measures of set-shifting ability; Trail Making Test (TMT), Wisconsin Card Sorting Test (WCST), Brixton task (BT), Haptic Illusion Task (HIT), CatBat task (CBT), Picture Set Test (PTS); Verbal Fluency Task (VFT); Intra-Extra Dimensional Set Shifting Test (ID/ED Shift Task); and Affective Shifting Task (AST) used for meta-analyses. The outcome variable was performance on the set-shifting aspect of the task. Effect sizes (Hedges's g) were pooled using fixed-effects models.

Results: Twenty-one studies were examined with a total of 514 BN patients and 939 healthy control groups. There was a small effect of BN diagnosis on set-shifting (Hedges's g = 0.24).

Conclusion: Based on the findings, problems in set-shifting as measured by a variety of neuropsychological tasks are present in people with bulimia nervosa.

Keywords: Bulimia nervosa, Cognitive flexibility, Meta-analysis, Set-shifting

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Introduction

Nutrition can significantly change a person's health by affecting all body parts. However, some inappropriate eating habits and psychological problems can lead to Eating Disorders (ED), including Bulimia Nervosa (BN) (1). Bulimia nervosa is defined by recurrent episodes of binge eating regularly occurring with inappropriate compensatory behavior from twice a week to once a week for at least three months. Bulimia nervosa is among the most common eating disorders and is the second most prevalent psychiatric problem among young women (2).

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The lifetime prevalence rate for bulimia nervosa in the United States is approximately 1.0%; however, rates are much higher in females than males (3.5% versus 0.9%, respectively) (3). The BN is ten times more common in females than males (4). Studies conducted on different groups in Iran showed that the prevalence of this disorder was %3.3 to 7% in female college students (5) and %1.2 to 2.3% in female school students (6).

This disorder is often chronic, relapsing, and devastating (2). Moreover, the pathogenesis is poorly understood, and robust etiological models to guide treatment are lacking. (7). Meanwhile, risk assessments in people with bulimia nervosa identify a wide range of factors, but these are not directly related to symptom expression and development (8). A recent approach to etiological understanding and treatment development is the examination of neurocognitive correlations (9).

Some scholars believe that executive dysfunction may exacerbate the intensity of thoughts and behaviors associated with bulimia nervosa (10), which may be evidenced by the inability of BN in set-shifting (11). He set-shifting difficulty is implicated as a potential risk marker, candidate endophenotype, and maintaining factor in EDs (12). Set-shifting is the ability to move between ideas, concepts, or tasks fluidly, such that those who have poor set-shifting are characterized by perseverative and rigid styles and behaviors (13). Problems in set-shifting may manifest either as cognitive inflexibility (e.g., concrete and rigid approaches to problem-solving and stimulus-bound behavior) or response inflexibility (e.g., perseverative or stereotyped behaviors) (14).

There is also the suggestion that set-shifting may be part of the eating disorder endophenotype, as deficits in set-shifting have been found in both affected and unaffected sister pairs (15).

Poor set-shifting is reported in adults with BN (16). However, the systematic review suggests that findings are mixed, and there are quite limited data on BN-type ED Not Otherwise Specified (EDNOS-BN). In general, there seems to be a widely recognized deficit in the literature on the relationship between neurocognition and bulimic syndromes (17).

Over the past 20 years, studies on the ability of set-shifting in BN patients have yielded conflicting results. However, some studies have suggested that a problem with set-shifting may be a part of the risk factors for developing a BN (18-20), which may be linked to compulsive traits, rigidity, and perfectionism (21). However, no significant difference was found between BN patients and normal individuals in set-shifting tasks (13,22,23).

Several systematic reviews and meta-analyses have also been conducted, but they have examined all eating disorders (16) or all executive actions (10). In this regard, a review of 15 studies on ED patients showed a small negative effect on set-shifting flexibility (standardized mean difference= −0.36) (16).

To our knowledge, no systematic reviews or meta-analyses have been conducted so far to examine set-shifting ability, specifically in BN patients. To fill this substantial gap, as well as to provide an update on the findings within this growing field of study, the present systematic review and meta-analysis utilized the sample of studies that have investigated this construct to date to calculate the effect size of bulimia nervosa diagnoses, which have been the primary focus on BN studies comparing set-shifting in BN diagnosed patients and healthy groups by employing cognitive performance measures. This systematic review and meta-analysis aimed to collate and summarize the literature on set-shifting ability in people with bulimia nervosa

Materials and Methods

We used The Preferred Reporting Items for Systematic Reviews and Meta-Analyses ("PRISMA") Statement guidelines to conduct this meta-analysis (24). Relevant studies were located through searches conducted in PubMed, PsycINFO, Scopus, and Google Scholar databases from the earliest date of publication covered by each through November 2019 (2002-2019).

Keywords used for searching included; NEUROPSYCHOLOGY, SET SHIFTING, FLEXIBILITY, RIGIDITY, MENTAL FLEXIBILITY, COGNITIVE RIGIDITY, PERSEVERATION, WISCONSIN CARD SORTING TEST, TRAIL MAKING TEST, BRIXTON, HAPTIC, CATBAT, EATING DISORDER, ANOREXIA NERVOSA, and BULIMIA NERVOSA. No date restrictions were applied to the selection of literature. Any study employing the set-shifting tasks Trail Making Test (TMT), Wisconsin Card Sorting Test (WCST), Brixton task (BT), Haptic Illusion Task (HIT), CatBat task (CBT), Picture

Set Test (PTS); Verbal Fluency Task (VFT); Intra-Extra Dimensional Set shifting Test (ID/ED Shift Task), and affective shifting task (AST) was eligible for inclusion. Although the specific operations involved may differ, all selected tasks require shifting between mental sets and strategies. The selection process and reasons for exclusion are depicted in Figure 1. The literature search resulted in a total of 1,349 articles being identified. Three more articles were identified through a search of reference lists. Once duplicates were removed, the title and abstract of the remaining 368 articles were screened for suitability for inclusion in the review. A total of 168 were excluded based on this screening process, leaving 101 articles for full-text review. After reviewing the full articles, a further 80 articles were excluded. This resulted in 21 articles possessing eligibility in the qualitative synthesis of this review. Finally, 15 articles were included in the qualitative synthesis of the meta-analysis. Figure 1 illustrates the flow of articles through this process.

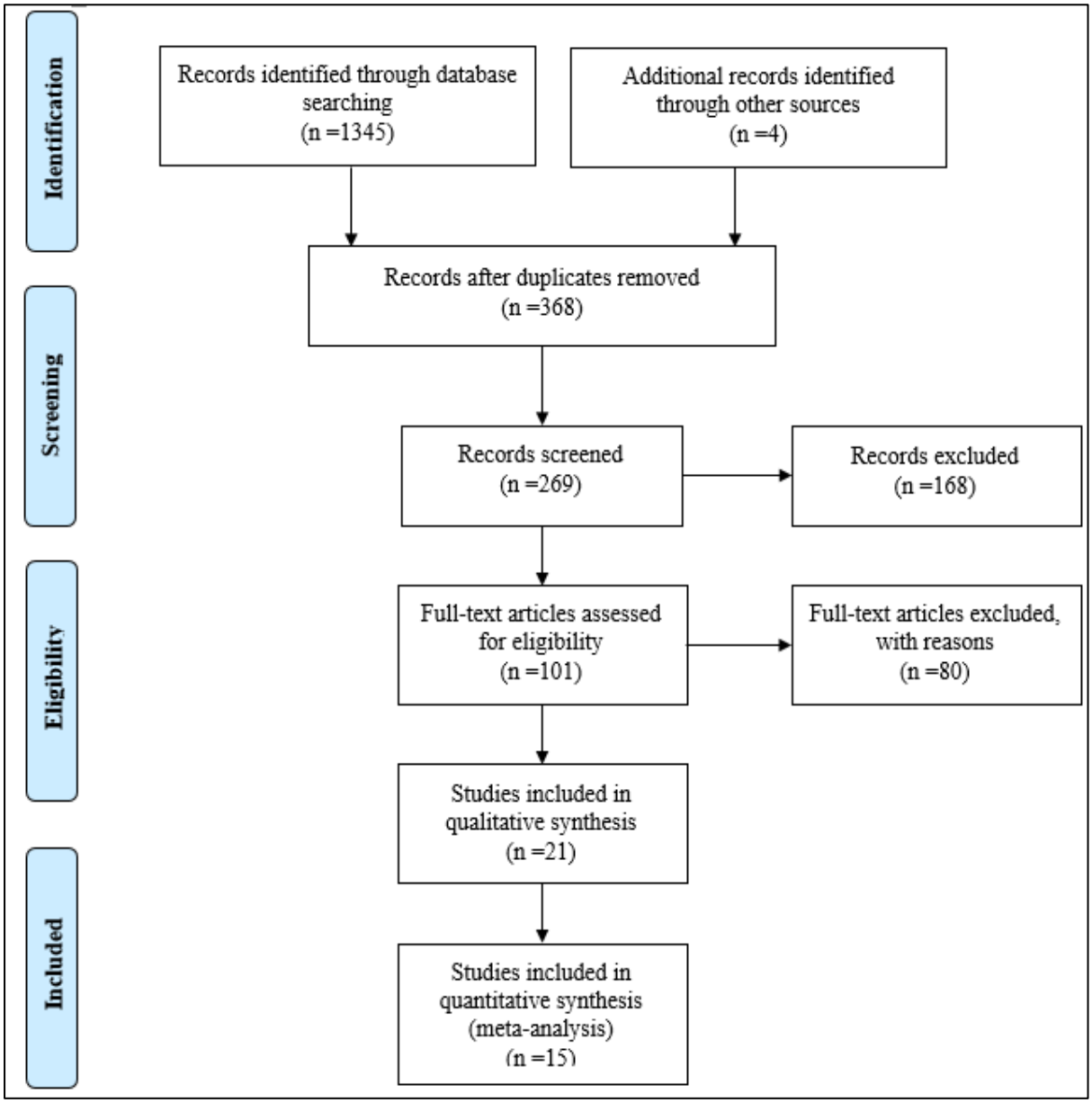

Figure 1. PRISMA 2009 flow diagram

Data analyses were conducted using the Comprehensive Meta-Analysis Version 3.0 software (25). In addition, two evaluators coded the selected articles separately using an election checklist of research projects.

Kappa coefficient of the evaluators' reliability was calculated at 0.79.

Results

1. Systematic review

Table 1. Articles on set-shifting and bulimia nervosa

Authors	Participants	Study design	Investigated areas	Tools	Main results
Brand et al., 2007	BN=14 HC=14	Casual-comparative	Neurological factors associated with decision making in BN patients	TMT	In the B task of TMT, BN group performed weaker than HC group.
Camacho Ruiz et al., 2008	BN=26 HC=36	Casual-comparative	Neurological findings on eating disorders	WCST	In WCST, BN group performed weaker than HC group.
Camacho Ruiz et al., 2012	BN=32 HC=32	Casual-comparative	New findings on BA neuroscience	WCST	In WCST, BN group performed weaker than HC group.
Darcy et al., 2012	BN=23 HC=22	Casual-comparative	Set-shifting in BN patients	A set of tests	No significant difference was found between BN and HC groups.
Degortes et al., 2016	BN=87 HC=159	Casual-comparative	Executive function in BN patients	WCST	In WCST, BN group performed weaker than HC group.
Galderisi et al., 2011	BN=83 HC=77	Casual-comparative	neuropsychological functions in bulimia nervosa	WCST	No significant difference was found between BN and HC groups in set-shifting task.
Galimberti et al., 2012	BN=16 HC=40	Casual-comparative	Motor inhibition and cognitive flexibility in various ED types	ID/ED Shift Task	No significant difference was found between BN and HC groups in set-shifting task.
Hirst et al., 2017		Meta-analysis	Meta-analysis of executive functions in AN and BN patients	WCST, TMT, Brixton	BN group performed weaker than HC group in TMT (g= -0.57) and WCST (g= -0.61, -0.80)
Jáuregui-Lobera et al., 2014		Systematic review	Executive function s involved in AN	TMT	In several studies, BN group performed weaker than HC group.
Kakoschke et al., 2019		Review	Cognitive deficits in compulsory eating behavior	-	In several studies, BN group performed weaker than HC group in set-shifting task; but others did not confirm it.
Kim et al., 2010	BN=28 HC=34	Casual-comparative	Set-shifting inability in ED patients	TMT	In TMT, BN group was weaker than HC group.
Mobbs et al., 2008	BN=18 HC=18	Casual-comparative	Cognitive deficit, with emphasis on set-shifting in MN patients	AST	In research task, BN group performed weaker than HC group.
Murphy et al., 2002	BN=16 HC=16	Casual-comparative	Conditional learning in AN	TMT	No significant difference in terms of set-shifting was found between BN and CH groups.
Pignatti et al., 2013	BN=17 HC=20	Correlational and casual-comparative	Factors affecting executive functions in ED	WCST, TMT	In WCST test, BN group was weaker than CG group.
Roberts et al., 2007		Systematic review and meta-analysis	Set-shifting in ED patients	TMT, WCST, CBT, HIT	A moderate and acceptable effect size was found for set-shifting task in BN group (0.17 to -1.05).
Roberts et al., 2010	BN=30 HC=88	Casual-comparative	Set-shifting in AN and BN patients	TMT, HIT, BT	In all tasks, BN group performed weaker than HC group.
Tchanturia et al., 2004	BN=19 HC=35	Casual-comparative	Cognitive flexibility in AN and BN patients	TMT, HIT, BT, PST, VFT, CBT	In CBT, VFT and PST tasks, BN group performed weaker than HC group.
Tchanturia et al., 2012	BN=82 HC=199	Casual-comparative	Cognitive flexibility in ED patients	WCST	In most WCST tasks, BN group performed weaker than HC group.
Vall et al., 2015	BN=23 HC=149	Casual-comparative	Performance of BN and AN patients in TMT	TMT	In TMT, BN group performed weaker than HC group.
Van den Eynde, 2011		Systematic review	Systematic review of neuropsychological functions in eating disorders	WCST, TMT, BT, HIT, CBT, PST	In two studies with WCST tasks, BN group performed weaker than HC group; but no significant difference was found in two studies. In BT task, no significant difference was found. Several findings confirmed weaker performance of BN group in TMT compared to HC group. In CBT, HIT and PST tasks, BN group performed weaker than HC group.
Wu et al., 2014		Meta-analysis	Set-shifting ED patients	-	A moderate difference was found between BN and HC groups in terms

of set-shifting (g= -0.50)

ED= Eating Disorders, AN= Anorexia Nervosa, BN= Bulimia Nervosa, CG= Control Group, HC= Healthy Control Group, NC= Normal Control AST= Affective Shifting Task; TMT=Trail Making Task; HIT= Haptic Illusion Task; BT= Brixton Test; PTS= Picture Set Test; VFT= Verbal Fluency Task; CBT= Cat Bat Task: ID/ED Shift Task= Intra-Extra Dimensional Set shifting Test

As presented in Table 1, articles in this study included 14 causal-comparatives, one correlation-causal-comparative, two meta-analyses, two systematic reviews, one review, and one systematic-meta-analysis review. In 11 studies, the BN group performed weaker than the healthy group in set-shifting tasks (12,18,19,26-33). In three meta-analyses, moderate (11) and moderate to high effect sizes were indicated (10,16).

However, some studies confirmed a significant difference between BN and HC groups in terms of set-shifting tasks (13,22,23,34).

2. Meta-Analysis

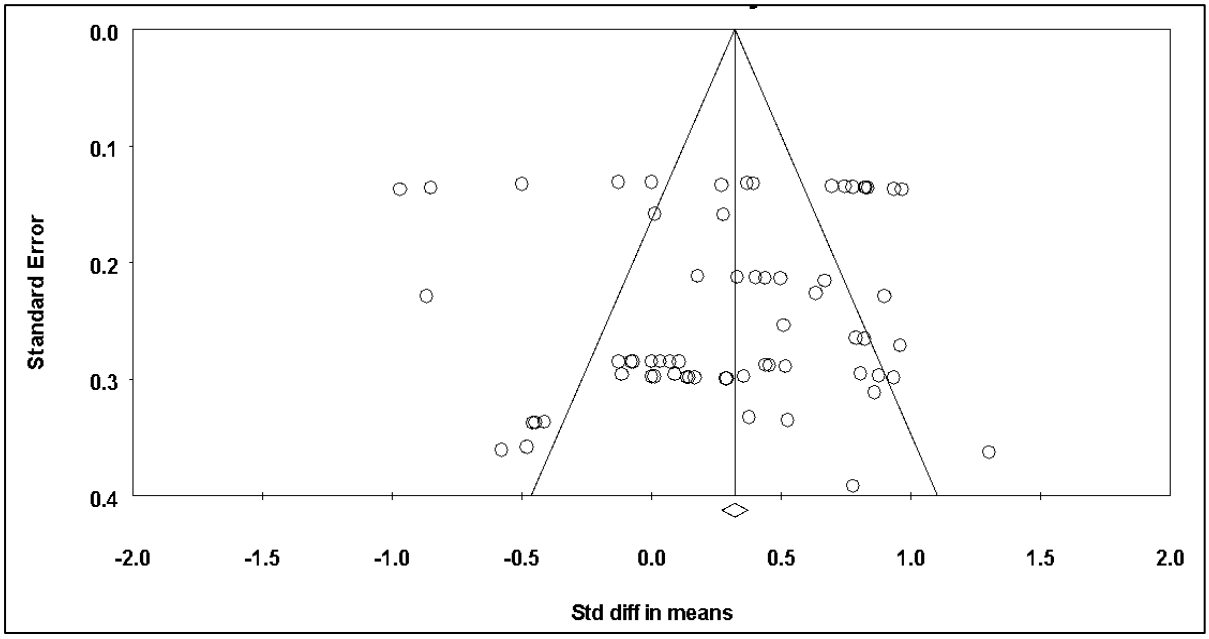

Figure 2. Funnel diagram before sensitivity analysis

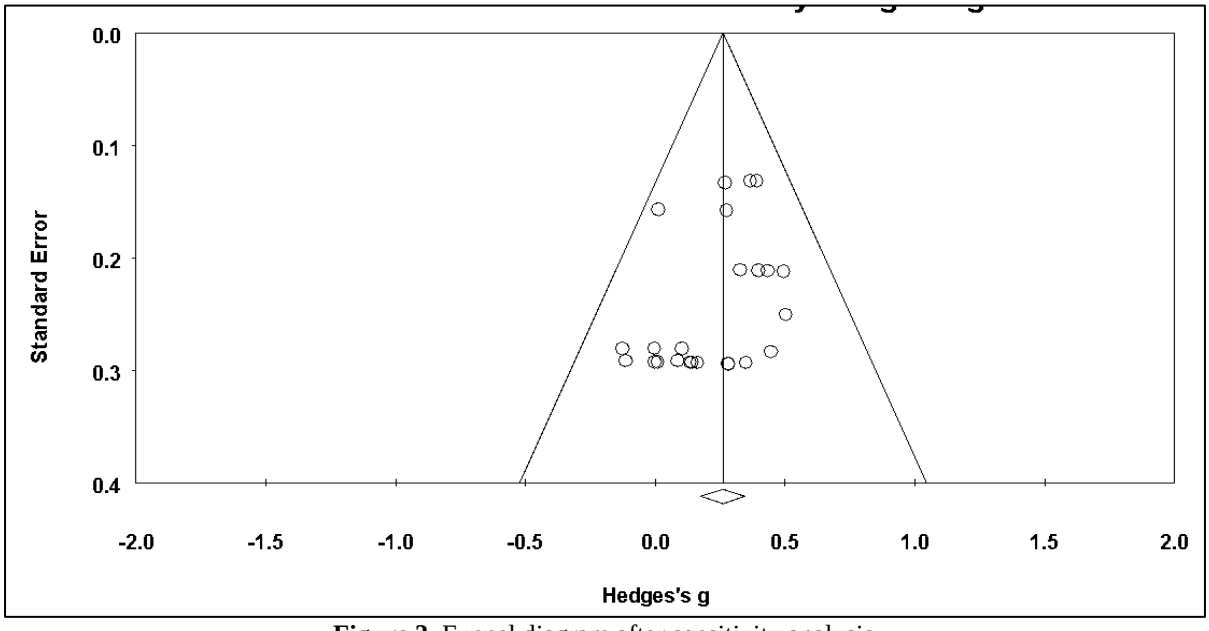

Figure 3. Funnel diagram after sensitivity analysis

Out of 67 effect sizes (Figure 2), 43 extreme ones were removed, and the remaining 24 were analyzed (Figure 3).

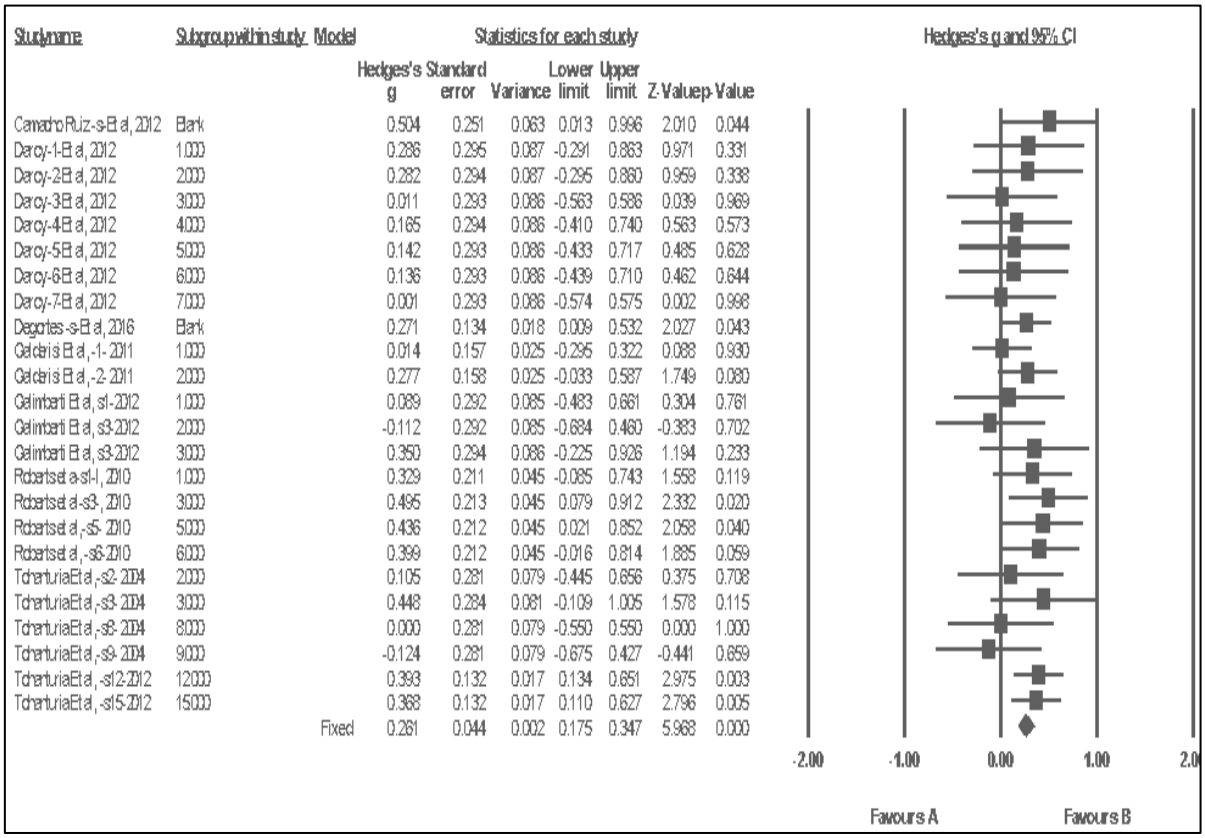

Figure 4. Effect size of set-shifting after sensitivity analysis

Table 2. Combined effect size of set-shifting and bulimia nervosa after sensitivity analysis

Model	N Studies	g	95% Confidence interval		Z	P	Test of homogeneity	
			Upper	Lower			Q	I
Fixed	24	0.26	0.34	0.17	5.96	0.001	14.92	0.00
Random	24	0.26	0.34	0.17	5.96	0.001		

After the sensitivity analysis, Table 2 shows combined fixed and random effects models related to 24 effect sizes. The mean combined effect size of set-shifting in bulimia nervosa in the fixed and random models is 0.26, which is statistically significant ($P< 0.01$). Therefore it can be concluded that set-shifting has a significant effect on bulimia nervosa. Also, given Cohen's criterion, this effect is small for both the fixed and random models. Therefore, set-shifting has a negligible effect size on BN.

Discussion

The meta-analysis results also revealed a small effect size between set-shifting and BN (Hedges's g= 0.24). Although set-shifting has been studied in different eating disorders groups, few review and meta-analysis studies have examined set-shifting specifically in BN patients. Results of a meta-analysis pointed to a moderate effect size of set-shifting on BN (Hedges's g= -0.50) (11). In another study, effect sizes of set-shifting varied based on different measurement tools (Hedges's g= 0.17-1.05) (16).

Effects of BN disorder on brain damage and other brain changes may be so firm that weaken the performance of patients diagnosed with BN in cognitive tests (7). In addition, it should be noted that many components of executive

functions, including impulse control, self-monitoring, and goal-oriented behavior are directly related to the ability to maintain set-shifting, and failure to acquire these skills during growth, directly or indirectly, is a risk factor for the development of eating disorders (35). In sum, the findings of the present review and meta-analysis demonstrated relevant set-shifting inefficiency in BN patients that may contribute to maladaptive eating behavior and prevent more flexible behavioral responses to environmental changes in general. Thus, psychological treatments for BN should not solely focus on disease-related issues (i.e., eating, weight, and shape) but could also target more basic cognitive control functions such as an inefficient set-shifting to remediate these specific inefficiencies in BN patients (36-38).

Also, set-shifting problems in BN may be a consequence of this disorder. Set-shifting may be due to the symptoms of BN (high-risk eating and clearing behavior); or it may be the comorbid effect of another disorder, such as perfectionism (39); or a conscious effort to increase dietary restriction to a diet that eventually leads to an overeating cycle in disorder, and then these dysfunctional efforts lead to the development of an inflexible nervous system that over time strengthens this dysfunctional nervous system (40). As well as disorders of the frontal lobe and other nerve areas of the brain present in these people; it reduces the ability to change the subject in these people. The limitations of the present study are: first, as with all meta-analyses, our findings are influenced by the characteristics of the primary studies to some degree. However, the sensitivity analysis indicates that study quality did not significantly influence the pooled overall BN. Second, again as with all meta-analyses, we cannot entirely exclude the possibility that publication biases confound the present meta-analysis results. However, we made some effort to minimize potential biases by additional searches for studies through contact with relevant research groups and exclusion of studies with patient samples overlapping with other reports. Furthermore, the funnel plots tests did not suggest a publication bias.

Third, although the tasks included in this review are considered typical set-shifting measures, our analyses revealed remarkably different BN patterns across these measures. The problems concerning the measurement of set-shifting have been discussed earlier. Fourth, our findings are only valid for BN patients. Furthermore, the results cannot be generalized to other EDs subgroups.

Conclusion

Based on the findings, it seems that problems in set-shifting as measured by a variety of neuropsychological tasks are present in people with bulimia nervosa.

Ethical considerations

This article was approved with the code of ethics IR.USB.REC.1399.026. The authors declare any conflict of interest.

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