

Evaluation of Cognitive-Behavioral Therapy Efficacy in the Treatment of Separation Anxiety Disorder in Childhood and Adolescence: a Systematic Review of Randomized Controlled Trials

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Abstract

Cognitive behavioral therapy (CBT) is a well-established treatment for anxiety disorders. However, few efforts have been made to summarize the impact of specific intervention-related variables on therapeutic outcomes in different-aged youth with a separation anxiety disorder (SAD). PRISMA guidelines were followed to provide an efficacy overview of different disorder-specific CBT protocols against transdiagnostic ones among youth with SAD. Literature search was conducted in Pubmed, EBSCOhost, PsychInfo, PsycArticles, PSYINDEX, Medline, and ERIC. In total, 9 papers met the eligibility criteria. Overall, preschoolers benefited more from disorder-specific CBT protocols, whereas school-aged children and adolescents from transdiagnostic ones. Interventions aimed at removing SAD maintenance factors, by including parent-sessions, were efficacious, especially among younger children. Psychotherapy had higher efficacy than drug treatments, with individual- and group-CBT addressing SAD symptoms similarly. Findings support CBT as the golden standard for SAD in youth, impacting on the core symptoms in a time-limited, goal-directed way, with long-term effects.

Keywords Anxiety · Cognitive-behavioural therapy · Separation · RCT design · Developmental psychopathology

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Introduction

Separation anxiety disorder (SAD) represents a public health priority worldwide, being the earliest and the most common anxiety disorder in childhood with estimated prevalence rates ranging from 2.6 to 5.2% in children younger than 12 years of age (Cartwright-Hatton et al., 2004; Ford et al., 2003; James et al., 2013; Kessler et al., 2005), accounting for one-half of the referrals for mental health treatment of anxiety disorders (Bell-Dolan, 1995; Cartwright-Hatton et al., 2006).

The overwhelming emotional distress, often associated with the core symptoms of SAD, and feelings of inability to function without caregiver's support, interferes with daily activities as well as developmental tasks, and undermines the child's social and academic functioning (Last et al., 1987; Scaini et al., 2020; Shear et al., 2006; Silverman & Niederhauser, 2004).

Evidence suggests that SAD in childhood may be a risk factor for a broad range of anxiety disorders, especially for panic disorder and agoraphobia (Battaglia et al., 1995), as well as mood disorders and substance addictions in late adolescence and early adulthood (Aschenbrand et al., 2003; Battaglia et al., 2009, 2017; Kossowsky et al., 2013; Lewinsohn et al., 2008; Woodward & Ferguson, 2001). Taken together, the high prevalence of SAD among youth, the associated impairments, and the negative mental health sequelae strongly highlight the need of identifying the type of treatment that might lead to additional benefits in therapeutic outcomes in different age groups (preschooler, schoolers, and adolescents).

The National Institute for Health and Care Excellence (NICE) guidelines included cognitive behavioural therapy (CBT) among the well-established and first-choice treatments for anxiety disorders in childhood and adolescence as its effectiveness has been extensively documented (Barrett et al., 1996a, b; Carpenter et al., 2018; Flannery-Schroeder & Kendall, 2000; Hofmann et al., 2012; James et al., 2013; NCCMH, 2011; Olatunji et al., 2010; Scaini et al., 2016; Walkup et al., 2008; Wang et al., 2017). However, as stated in several reviews and meta-analyses, up to 40% of children with a diagnosis of anxiety disorder do not recover following a standard and transdiagnostic CBT protocol (Cartwright-Hatton et al., 2004; Higa-McMillan et al., 2016; Silverman et al., 2008; Warwick et al., 2017). In this regard, disorder-specific CBT protocols for children have been developed for obsessive-compulsive disorder (Derisley et al., 2008; March & Mulle, 1998), post-traumatic stress disorder (Cohen et al., 2000; Smith et al., 2007), social anxiety disorder (Fisher et al., 2004), specific phobias (Davis et al., 2009), and separation anxiety disorder (Blatter-Meunier & Schneider, 2011) but it is unclear if disorder-specific CBT interventions, targeting the core features of the disease, might enhance the rates of anxiety symptoms' reduction and diagnosis remission compared to transdiagnostic ones, such as the Coping Cat Program (CC: Kendall, 1994). The recent review of Oldham-Cooper and Loades (2017) has pointed out that the transdiagnostic CBT protocol, namely CC, was equally effective as disorder-specific treatments for SAD among youth aged between 7 and 17 years. However, the paucity of studies regarding the differential efficacy of

standard CBT against disorder-specific CBT for SAD does not allow drawing firm conclusions. Several studies supported strong evidence-based use of disorder-specific approaches for the treatment of anxiety disorders in childhood and adolescence (Butler et al., 2010; Kendall, 1994; Reynolds et al., 2012; Scaini et al., 2016). Nonetheless, to our knowledge, no studies compared them to treatment that might lead to the best possible outcomes across age groups.

Furthermore, several etiological researches indicate that parental behaviors and cognitions may act as crucial maintenance factors for SAD (Barrett et al., 1996a,b; Caputi et al., 2020; Cobham et al., 1998; Herren et al., 2013), emphasizing that they could facilitate avoidance patterns and cognitive biases in their children throughout reinforcement and modelling (Barrett et al., 1996a, b; Scaini et al., 2018). Higher levels of parental anxiety have been associated with poorer youth outcomes after CBT (Berman et al., 2000; Crawford & Manassis, 2001; Southam-Gerow et al., 2001), limiting the generalization of the child's treatment gains in real-world settings (Ginsburg et al., 2004; Wood et al., 2003). The pilot study of Choate et al. (2005) offered encouraging efficacy results about the application of the Parent-Child Interaction Therapy (PCIT) to three families with a child aged between 4 and 8 years who had a principal diagnosis of SAD, as incidence of separation anxiety symptoms dropped to zero at post-treatment and remained at or close to it at 3-month follow-up. These findings are promising in suggesting that PCIT may be an effective treatment for pre-schoolers experiencing SAD and delineate the importance of incorporating parent-sessions to foster the reduction of child separation anxiety and disorder-related impairments. However, as the authors stated, further investigations with randomized controlled trials (RCTs) are warranted to investigate treatment gains generalizability. The meta-analysis carried out by Brendel and Maynard (2014) outlined that parent-child interventions appear to be more effective than child-focused individual and group CBT in treating childhood anxiety disorders, acknowledging the role of parental involvement in enhancing therapeutic efficacy. In contrast, other meta-analyses (Reynolds et al., 2012; Silverman et al., 2008; Thulin et al., 2014; Wergeland et al., 2021) showed that CBT programs with and without active parental involvement show comparable efficacy at post-treatment.

To date, only six studies (de Groot et al., 2007; Flannery-Schroeder & Kendall, 2000; Flannery-Schroeder et al., 2005; Liber et al., 2008; Manassis et al., 2002; Muris et al., 2001) directly compared the efficacy of the two abovementioned CBT modes of delivery for AD and none of them reported relevant differences in treatment outcomes. Therefore, the two therapeutic approaches appear to be comparable for a wide spectrum of AD. Controversial results emerged only concerning social anxiety disorder (SoP). On one hand, Manassis et al. (2002) pointed out greater treatment gains for children with SoP in individual CBT (ICBT) compared to group CBT (GCBT); on the other hand, Liber et al. (2008) reported higher diagnostic recovery rates in children treated with GCBT, stating the supremacy of the latter over ICBT. Concerning SAD, few efforts have been made to outline whether ICBT or GCBT is more efficacious in addressing the core features of the disorder and to what extent different age targets may benefit from it (Barrett, 1998; Silverman et al., 1999). Finally, there is evidence that pharmacotherapy is better viewed as an additional therapy rather than as a first treatment option for

SAD, in children not responding to other interventions (Bernstein & Shaw, 1997; James et al., 2013; Masi et al., 2001). The selective serotonin reuptake inhibitors (SSRI) are considered the first-line drug treatment for anxious children and adolescents by the Food and Drug Administration (Baldwin et al., 2005; Patel et al., 2018). However, even though such medications are widely prescribed for youth with AD, data proving their efficacy is still scant compared to other well-established psychological treatments (Avari et al., 2019), and little is known about the relative efficacy of pharmacotherapy against psychotherapy and combined treatment for SAD.

As stated above, to our knowledge, few efforts have been made to replicate the efficacy studies of different CBT modes of delivery for AD in youth affected by SAD. Although a growing body of literature supports the use of individual, group, family-based, transdiagnostic, and disorder-specific CBT protocols for AD treatment (Butler et al., 2006; Cuijpers et al., 2016; Ewing et al., 2015; Sigurvinsdóttir et al., 2020), CBT adjustments to different age groups are still debated (James et al., 2013).

In light of these premises, the current review is aimed at investigating whether transdiagnostic CBT protocols have higher clinical efficacy and effectiveness compared to disorder-specific ones in reducing SAD symptoms and fostering SAD diagnosis remission in children and adolescents. Moreover, this review is also aimed at acknowledging the role of parental involvement in enhancing the therapeutic efficacy of child-based CBT protocols and examining the first-choice treatments between CBT individual and group format. Finally, three modes of delivery will be compared and contrasted: monotherapies (psychotherapy and pharmacotherapy) and combined treatment.

Method

The present systematic review was written according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA-P, Shamseer et al., 2015) guidelines.

Information Sources and Search Strategy

Relevant studies were identified through an extensive search in the following electronic databases: Pubmed, EBSCOhost, PsychInfo, PsycArticles, PSYINDEX, Medline, and ERIC using “Separation anxiety disorder” AND “Cognitive-Behavioral Therapy” AND “Efficacy” OR “Effectiveness” AND “Children” OR “Adolescents” AND “Clinical trials” NOT “Trauma” as keywords. The last search term was specified to exclude all those studies considering the onset of anxiety symptoms as a reactive response to the exposure to stressful and traumatic events. Additional relevant literature was selected through a manual screening of reference lists. We included literature up to May 2021.

Study Selection, Data Collection Process, and Eligible Studies Included

The selection of studies and data collection process started with the analysis of the articles' title aimed at identifying duplicates to remove (see Fig. 1), followed by the screening of abstracts to determine the content suitability of the paper with the topic of this review. The following inclusion criteria were applied to the literature search: (i) randomized controlled trials (RCTs) study design; (ii) SAD diagnosis remission and SAD symptoms reduction as first outcome measure; (iii) sample composed of children and/or adolescents aged between 4 and 18 years old with a primary DSM-based diagnosis of SAD; (iv) English as the language of publication; and (v) date of publication later 1994 (Kendall, 1994). Studies on participants with a comorbid diagnosis of intellectual disability, psychosis, bipolar disorder, and suicidality, as well as those aimed at testing the efficacy of

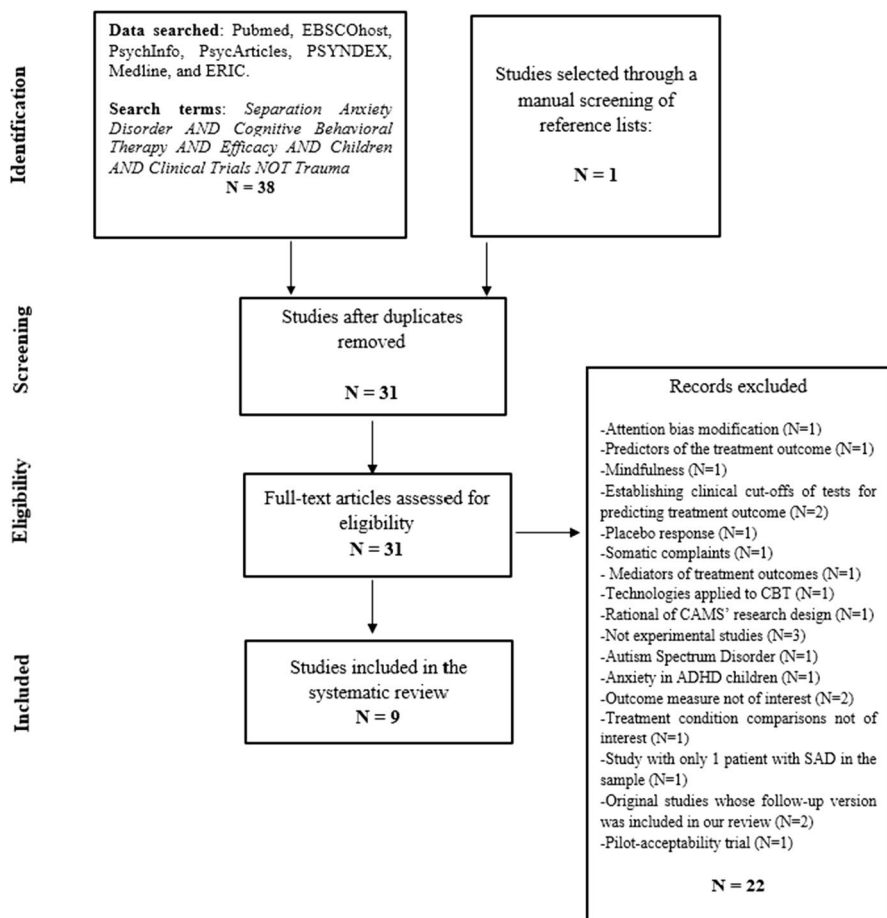


Fig. 1 PRISMA literature search flow diagram

transdiagnostic CBT protocols with waitlist-controls, were excluded. Reviews and meta-analyses were also excluded. After applying the aforementioned criteria, 31 articles were detected and assessed in depth. Subsequently, 22 studies were excluded. Of these, 20 studies were out of topic as they were not aimed at testing the efficacy of different formats of CBT protocols for SAD treatment in children and adolescents, considering diagnosis remission and anxiety symptoms reduction rates as first outcome measures. The remaining two studies were excluded as we included the updated version with follow-up assessments of the original data (Walkup et al., 2008; Wergeland et al., 2014). In the end, nine studies met eligibility criteria and were included in the systematic review. The descriptive characteristics of the RCT studies analyzed are summarized in Table 1.

Data Extraction

Two authors (LG and SC) independently inspected and screened all full reports identified by the search. Disagreement regarding eligibility was resolved by consensus (intercoder reliability: Cohen's Kappa coefficient = 0.85). With regard to the process of data extraction from the selected studies, the following data were extrapolated: (i) the type of treatment administered to patients; (ii) the kind of treatment comparisons assessed; (iii) trial design; (iv) duration of post-treatment and follow-ups; (v) instruments administered; (vi) primary DSM-based diagnosis of patients; (vii) patients' age; and (viii) rates of SAD symptoms reduction, analyzing score changes in self-report, parent-report and teacher-report questionnaires, and SAD diagnosis remission among different time-points of evaluation as main outcome measures of CBT treatment efficacy and/or effectiveness. Either data about the remission of all anxiety diagnoses or the primary anxiety diagnosis at post-treatment and follow-up were extracted, in case of availability.

Data Synthesis

The included studies were highly heterogeneous in terms of treatment comparisons, the age range of participants, and instruments administered. Studies were grouped and analyzed based on the characteristics of patients involved in the RCTs, and the type of treatment comparisons that were carried out. The primary outcome comprised a dichotomous outcome (diagnostic remission vs no remission) that was synthesized reporting the rate of patients fulfilling diagnostic criteria for SAD at baseline and remitting at post-treatment/follow-up. Continuous measures were aggregated and synthesized either quantitatively or qualitatively. We reported means and standard deviations of scores obtained in the administered tests, to highlight the trend of symptomatology across time in the different treatment conditions. In the absence of quantitative data, we operated a qualitative synthesis of the main results, specifying how symptoms changed after treatment across age groups.

Table 1 Descriptive core features of the RCT studies analyzed in the present systematic review

Author	Target disorder	Rand-omized sample N	Mean age in years (SD; range)	Gender % female	Study Design	Type of treatment	Treatment conditions
Hirshfeld-Becker et al. (2010)	SAD, social anxiety disorder/SoP, agoraphobia, GAD, SP	64	5.4 (1.0; 4–7)	53%	RCT	Transdiagnostic	Being brave: a parent-child CBT protocol
Kendall et al. (2008)	SAD, GAD, SP	161	10.27 (NR; 7–14)	44%	RCT	Transdiagnostic vs disorder-specific CBT	ICBT, FCBT, FESA
Kodal et al. (2018)	SAD, GAD, social anxiety disorder/SoP	139	15.5 (2.5; 11–20)	54.7%	RCT	Transdiagnostic	ICBT, GCBT
Santucci and Ehrenreich-May (2013)	SAD	29	9.18 (1.58; 7–12)	100%	RCT	Disorder-specific CBT	The Child Anxiety Multi-Day Program for SAD; intensive context-adapted CBT
Schneider et al. (2011)	SAD	43	SAD: 6.29 (1.01; 5–7) WL: 6.18 (0.73; 5–7)	NR	RCT	Disorder-specific CBT	TAFF
Schneider et al. (2013)	SAD	64	10.36 (1.55; 8–13)	51.5%	RCT	Transdiagnostic vs disorder-specific CBT	CBT (Coping Cat program), TAFF
Piacentini et al. (2014)	SAD, GAD, social anxiety disorder/SoP	488	10.7 (2.8; 7–17)	50%	RCT	Transdiagnostic	CBT (Coping Cat program), SRT, COMB, PBO
Villabø et al. (2018)	SAD, GAD, social anxiety disorder/SoP	165	10.46 (1.49; 7–13)	55.5%	RCT	Transdiagnostic	ICBT, GCBT
Walczak et al. (2017)	SAD, GAD, SP, social anxiety disorder/SoP	54	Younger children: 8.86 (1.46; 7–9); older children: 9.85 (1.76; 10–12)	NR	RCT	Transdiagnostic vs disorder-specific CBT	CBT with active parent involvement vs standard CBT with limited parent involvement

NR, not reported; SAD, separation anxiety disorder; GAD, generalized anxiety disorder; SP, specific phobia; TAFF, Separation Anxiety Family Therapy; ICBT, individual/child-based cognitive behavioral therapy; FCBT, family cognitive behavioral therapy; FESA, family-based education support attention; GCBT, group cognitive behavioral therapy; SRT, sertraline; COMB, combined treatment; PBO, placebo; WL, waitlist

Results

A total of nine studies, meeting eligibility criteria, was found (see Table 1). In particular, two studies evaluated the efficacy of a disorders-specific CBT protocol to address the core psychopathological features of SAD; three studies focused on comparing the efficacy of transdiagnostic CBT protocols against disorder-specific formats characterized by the inclusion of target parent-sessions; five studies analyzed the role of parental involvement in CBT on the changes of child diagnostic status and symptomatology; one study compared the efficacy of monotherapies, such as CBT and pharmacotherapy, with the combined treatment; and two studies compared ICBT with GCBT. Moreover, four out of the nine selected studies have focused solely on SAD, whereas the remaining eight studies also included patients with other anxiety disorders, basically generalized anxiety disorder (GAD), social anxiety disorder (SoP), and specific phobia (SP) (Tables 2 and 3).

CBT Clinical Efficacy

Overall, the selected studies provide evidence that CBT is a well-established efficacious treatment (Silverman & Hinshaw, 2008) for SAD in childhood and adolescence as it is associated with significant separation anxiety symptoms' reduction and diagnostic recovery rates. CBT successfully addresses the core symptoms of SAD in a time-limited and goal-directed way, and reduces psychosocial impairments in several functioning daily areas, as emerged among different raters, either when offered individually or as a parent-child treatment. Moreover, treatment gains are likely to be longstanding till 3-year follow-up, paving the way for promising low rates of relapse.

Disorder-Specific CBT

The studies that tested the clinical efficacy of a disorder-specific CBT protocol focused on pre-schoolers and schoolers comparing diagnosis remission and symptoms reduction rates against waitlist controls (Santucci & Ehrenreich-May, 2013; Schneider et al., 2011). The randomized controlled trial carried out by Santucci and Ehrenreich-May (2013) showed that treatment gains of an intensive disorder-specific CBT program in children aged between 7 and 12 years old were evidenced by changes in diagnostic status at post-treatment ($t_{(13)} = 5.98, p < 0.001$) and 6-week follow-up ($\chi^2_{(1)} = 8.78, p < 0.01$), as well as significant reductions in avoidance behavioral patterns, and improvements on parent-report (SCAS-P SAD, $F_{(1,23)} = 4.33, p < 0.05, \eta^2 = 0.16$) but not on child self-report (SCAS-C SAD, $F < 1.10, p > 0.31$) about separation anxiety symptomatology. In particular, 61% of children no longer met diagnostic criteria for SAD at follow-up (Santucci and Ehrenreich-May, 2013) compared to the 76.19% identified by the second mentioned study (Schneider et al., 2011) that enrolled children aged between 5 and

Table 2 Analysis of the diagnostic remission rates in the selected studies

Author	Diagnostic status			No diagnosis	FU
	Measure	Definition	Post-treatment		
	Age range				
Hirshfeld-Becker et al. (2010)	K-SAD-E 4–7 years	Remission of all anxiety diagnoses	59%	1-year FU, 59%	
Kendall et al. (2008)	ADIS-C/P 7–14 years	Remission of primary AD diagnosis	ICBT vs FCBT vs FESA: 64% vs 64% vs 42% FESA: 67% vs 64% vs 46%	1-year FU, ICBT vs FCBT vs FESA: 67% vs 64% vs 46%	
Kodal et al. (2018)	ADIS-C/P 11–20 years	1) Remission of all anxiety diagnoses 2) Remission of primary anxiety diagnosis	ICBT vs GCBT: 1) 31.4% vs 23.3% 2) 42.9% vs 37.7%	3.9-year FU, ICBT vs GCBT: 1) 55.7% vs 49.3% 2) 65.7% vs 59.4%	
Santucci and Ehrenreich-May (2013)	ADIS-C/P 7–12 years	Remission of SAD diagnosis	43%	6-week FU, 61%	
Schneider et al. (2011)	Kinder-DIPS 5–7 years	Remission of SAD diagnosis	/	1-month FU, 76.19%	
Schneider et al. (2013)	Kinder-DIPS 8–13 years	Remission of SAD diagnosis	TAFF vs CC: 87.5% vs 82.1%	1-year FU, TAFF vs CC: 83.3% vs 75%	
Piacentini et al. (2014)	ADIS-C/P 7–17 years	Remission diagnosis	COMB vs CBT vs SRT vs PBO: 80.7% vs 59.7% vs 54.9% vs 28.3%	36-week FU, COMB vs CBT vs SRT: 83% vs 80% vs 82%	
Villabø et al. (2018)	ADIS 7–13 years	Remission of SAD diagnosis	ICBT vs GCBT: 52% vs 65%	Maintenance of treatment gains at 2-year FU	

Table 2 (continued)

Author	Diagnostic status		
	Measure	Definition	No diagnosis
Walczak et al. (2017)	ADIS-IV-C/P	1) Remission of all anxiety diagnoses 2) Remission of primary anxiety diagnosis	1) Limited vs active parental involvement: 47.1% vs 34.8% 2) Limited vs active parental involvement: 52.9% vs 56.5%
	Age range	7–12 years	Post-treatment
			FU
			6-month FU, limited vs active parental involvement: 1) 82.4% vs 52.2% 2) 88.2% vs 69.6%
			3-year FU, limited vs active parental involvement: 1) 58.8% vs 73.9% 2) 82.4% vs 87.0%

FU, follow-up; *K-SAD-E*, child version of the Schedule for Affective Disorders and Schizophrenia, Epidemiologic version for DSM-IV; *ADIS-C/P*, Anxiety Disorder Interview Schedule, Child and Parent version; *ADIS-IV-C/P*, Anxiety Disorder Interview Schedule for DSM-IV, Child and Parent version; *Kinder-DIPS*, Diagnostic Interview for Children and Youth; *ICBT*, individual/child-based cognitive behavioral therapy; *FCBT*, family cognitive behavioral therapy; *FESA*, family-based education support attention; *GCBT*, group cognitive behavioral therapy; *SRT*, sertraline; *COMB*, combined treatment; *PBO*, placebo; *TAFF*, Separation Anxiety Family Therapy

Table 3 Analysis of the reduction symptomatology rates in the selected studies

Author	Anxiety outcomes		Non anxiety outcomes				
	Age range	Measure	Post-treatment	Measure			
Hirshfeld-Becker et al. (2010)	4 – 7 years	CBCL-int	Decrease: From 65.92 ± 7.71 to 58.90 ± 10.10 in CBT vs from 63.32 ± 8.02 to 60.69 ± 8.11 in controls ($p = .157$)	CQ	Increase: from 2.41 ± .55 to 4.48 ± 1.15 in CBT vs from 2.21 ± .66 to 3.45 ± .85 in controls ($p = .009$)	FU	/
Kendall et al. (2008)	7 – 14 years	MASC	Decrease in all treatment conditions ($p < .001$)	CGI	Improvement in SAD children: from 1.67 ± .98 to 2.46 ± .88 ($p = .045$)	FU	83% of treated children were rated as very much or much improved
		Parent-report CBCL-A	Decrease in mother and father-reports in all treatment conditions ($p < .001$)	CQ-C	Increase in all treatment conditions ($p < .001$)		Increase in all treatment conditions ($p = .001$)
		Teacher-report CBCL-A	Decrease in mother and father-reports in all treatment conditions ($p < .001$)	CQ-P	Increase in all treatment conditions ($p < .001$)		Increase in all treatment conditions ($p < .001$)
			Higher decrease in ICBT than in FCBT				
Kodal et al. (2018)	11 – 20 years	SCAS-C/P	Decrease in child and parent-reports in both treatment conditions	/	/	/	/

Table 3 (continued)

Author	Anxiety outcomes		Non anxiety outcomes		
	Age range	Measure	Post-treatment	Measure	
Santucci and Ehrenreich-May (2013)	7 – 12 years	SCAS-C/P SAD	Child version: decrease from 8.36 ± 3.61 to 6.93 ± 3.10 ($p = .73$)	CGAS	Increase: from 60.79 ± 7.26 to 70.43 ± 9.91 ($p < .01$)
			Parent version: decrease from 10.14 ± 2.41 to 8.86 ± 2.48 ($p < .05$)		
Schneider et al. (2011)	5 – 7 years	SAI	Child version: decrease from 2.13 ± .99 to .87 ± .90 ($p < .05$)	IQL	/
			Mother version: decrease from 2.59 ± .76 to 1.53 ± .69 ($p < .001$)		
			Father version: decrease from 2.57 ± .83 to 1.61 ± .69 ($p < .001$)		

Table 3 (continued)

Author	Anxiety outcomes		Non anxiety outcomes	
	Age range	Measure	Post-treatment	Measure
			FU	FU
Schneider et al. (2013)	8 – 13 years	SAAI-C/P	Decrease in all treatment conditions and across all raters but SAAI ratings in mothers decreased faster in TAFF than in CC	At 1-month FU and 1-year FU no differences between TAFF and CC for any rater
Piacentini et al. (2014)	7 – 17 years	PARS	/	Decrease in all treatment conditions ($p < .05$)
Villabø et al. (2018)	7 – 13 years	MASC	No differences in MASC scores in the treatment conditions for child and parent reports	Continuous increase on MASC scores in GCBT ($p < .001$), but not in ICBT ($p = .216$)
Walczak et al. (2017)	7 – 12 years	/	/	CGI-S / CGAS / No differences in CGAS scores in the treatment conditions for child and parent reports
				CGI-S / CGAS / No differences in CGAS scores in the treatment conditions for child and parent reports

CBCL-int: Child Behavior Checklist internalizing subscale; *CBCL-A*: Child Behavior Checklist anxiety symptoms; *CQ*, Coping Questionnaire; *CQ-C*, Coping Questionnaire, child version; *CQ-P*, Coping Questionnaire, parent version; *CGI*, Clinical Global Improvement; *MASC*, Multidimensional Anxiety Scale for Children; *SCAS-C/P* *SAD*, Spence Children's Anxiety Scale, child and parent version for Separation Anxiety Disorder; *CGAS*, Global Assessment Scale for Children; *SAI*, Separation Anxiety Inventory for Children; *IQL*, Assessment of Quality of Life in children, and adolescents; *SAAI-C/P*, Separation Anxiety Avoidance Inventory for Children, child and parent version; *PARS*, Pediatric Anxiety Rating Scale; *CGI-S*, Clinical Global Impression Severity Scale

7 years old in TAFF, suggesting a better efficacy of disorder-specific CBT protocols in younger children among pre-schoolers and schoolers.

Comparison Between Transdiagnostic CBT Protocols and Disorder-Specific Ones

Three studies (Kendall et al., 2008; Schneider et al., 2013; Walczak et al., 2017) compared transdiagnostic CBT protocols with disorder-specific ones among schoolers and pre-adolescents, aged between 7 and 14 years, and provided a common line of evidence in terms of clinical efficacy. In particular, the study of Schneider et al. (2013) reported that at 1-month follow-up, 87.5% of children assigned to the Separation Anxiety Family Therapy (TAFF) cohort, and 82.1% of children treated with the Coping Cat (CC) program recovered from SAD diagnosis. However, no between-group differences were detected at this time-point of assessment ($\chi^2_{(1, 52)} = 1.42, p = 0.23$). At 1-year follow-up, 83.3% of TAFF children and 75% of CC children kept on no longer fulfilling SAD diagnostic criteria ($\chi^2_{(1, 45)} = 3.51, p = 0.061$). Results indicate a slight advantage of TAFF program over a general child-based treatment for SAD. However, differences in diagnosis remission rates were less strong than hypothesized. Similarly, the study of Kendall et al. (2008) pointed out the absence of statistically significant differences in principal diagnosis remission rates between individual-CBT (ICBT) and family-based CBT (FCBT) at post-treatment (64% vs 64%, $\chi^2_{(2, 198)} = 7.84, p > 0.05$) and 1-year follow-up (67% vs 64%, $p > 0.05$). On that line of evidence, the randomized controlled trial carried out by Walczak et al. (2017) outlined that 87% of children enrolled in the disorder-specific CBT protocol with active parental involvement and 82.4% of children treated with the standard CBT with limited parental involvement were free of primary anxiety diagnosis at 3-year follow-up, but no differences were detected among treatment conditions ($p = 0.687$). Relevant differences emerged between 6-month and 3-year follow-ups where children exposed to disorder-specific CBT experienced higher diagnosis remission rates than children assigned to standard CBT protocols with limited parental inclusion ($p = 0.007$). With regard to symptoms severity reduction among treatment conditions and across time-points of assessment, the study of Schneider et al. (2013) reported no statistically significant changes on global success ratings in child self-reports and parent self-reports among treatment conditions (CC vs TAFF, $p > 0.05$), except for father's rating at 1-year follow-up ($t_{(32)} = -2.23, p < 0.05, d = 0.37$). Both mothers and fathers reported a significant downward trend of anxiety symptoms across different time-points ($p < 0.01$) and an upward trend of child-coping strategies to face distress in challenging situations ($p < 0.01$) (Kendall et al., 2008). However, only according to teacher self-reports, ICBT protocols resulted in greater internalizing symptoms' severity reduction ($F_{(4, 187)} = 3.04, p < 0.05$) and anxiety symptoms reduction ($F_{(4, 162)} = 4.51, p < 0.05$) compared to FCBT (Kendall et al., 2008). In the study of Schneider et al. (2013), scores on the Separation Anxiety Avoidance Inventory (SAAI) decreased more in TAFF than in CC only according to the mother rater ($p < 0.01, d = 0.33$).

The Role of Parental Involvement in CBT

Five out of the nine selected studies have analyzed the role of parental involvement in CBT on the changes of child diagnostic status and symptomatology at post-treatment and follow-ups (Hirshfeld-Becker et al., 2010; Kendall et al., 2008; Schneider et al., 2011, 2013; Walczak et al., 2017). In particular, three of them focused on an overlapping age target, ranging from 7 to 14 years old (Kendall et al., 2008; Schneider et al., 2013; Walczak et al., 2017), whereas the remaining two studies explored the effects of parental involvement in younger children aged between 4 and 7 years (Hirshfeld-Becker et al., 2010; Schneider et al., 2011). Findings provide support to the notion that the introduction of target parent-sessions aimed at addressing well-established maintenance factors for anxiety disorders, like parental dysfunctional cognitions and reinforcement of avoidance behaviors, did not result in a major reduction of child SAD symptoms severity and higher remission rates of SAD diagnosis among schoolers and early adolescents (Kendall et al., 2008; Schneider et al., 2011, 2013), whereas major therapeutic benefits derived from parental involvement were encountered among pre-schoolers and younger children (Hirshfeld-Becker et al., 2010; Walczak et al., 2017).

Psychotherapy Versus Pharmacotherapy and Combined Treatment

The study of Piacentini et al. (2014) is the follow-up version (phase II) of the Child-Adolescent Anxiety Multimodal Study (CAMS), originally carried out by Walkup et al. (2008), that extended the efficacy evaluations beyond the 12 weeks of acute treatment (phase I). It was aimed at comparing the efficacy of monotherapies, such as CBT and pharmacotherapy, which imply the administration of the SSRI-antidepressant Sertraline, with the combined treatment (COMB) in a broad age-target (7–17 years). Results show that psychotherapy is associated with superior response rates at post-treatment, in terms of SAD diagnosis remission and symptoms' severity reduction, compared to the drug treatment (59.7% vs 54.9%, $p < 0.001$). The outcome measures of the combined treatment overcome the monotherapies' ones (80.7%, $p < 0.001$), thanks to the active principle of drug which allows a direct action on symptoms and their severity, increasing the likelihood of compliance to psychotherapy by the patient. The long-term maintenance of the following outcome measures was demonstrated with longer follow-ups at 24 and 36 weeks after the acute treatment phase that confirmed that COMB is more effective than monotherapies either in terms of diagnosis remission or anxiety symptoms reduction rates ($p < 0.001$), whereas psychotherapy outperforms drug treatment. However, responder rates for COMB held steady through weeks 24 and 36 while both monotherapies improved considerably at 36-week follow-up such that the superiority of COMB over CBT and Sertraline-based pharmacotherapy seen at post-treatment failed to achieve statistical significance at follow-up (Piacentini et al., 2014).

Group Versus Individual CBT

At the current state-of-art, both individual and group CBT proved to be effective in addressing the core symptoms and related impairments of SAD, with no overall significant differences between them, lending support to the efficacy and effectiveness of both formats of delivery in schoolers and adolescents (Kodal et al., 2018; Villabø et al., 2018). Specifically, the study of Villabø et al. (2018) pointed out that SAD diagnosis remission rates at 12-week post-treatment were 52% for ICBT, 65% for GCBT, and 14% for WL in children aged between 7 and 13 years old. However, despite the slight advantage of GCBT over ICBT, no relevant statistical differences in diagnostic outcome emerged between the two formats of CBT delivery ($p=0.19$). The absence of statistically significant differences between the two formats of CBT either in the diagnostic outcome or in the child and parent reports about separation anxiety symptomatology was also confirmed by the study of Kodal et al. (2018), that compared the long-term efficacy of the two CBT modes of delivery at 3.9-year follow-up, confirming the preliminary results emerged at post-treatment and 1-year follow-up from the main study by Wergeland et al. (2014).

Discussion

Even if the number of studies that met eligibility criteria for the present review was small and great heterogeneity existed between transdiagnostic and disorder-specific CBT protocols administered, encouraging results emerged. Overall, the selected studies support the existence of different CBT formats able to effectively address the core symptoms of SAD and to reduce psychosocial impairments and restrictions linked to the disorder in several functioning daily areas. Findings of this review replicated and extended that of earlier reviews and meta-analyses by Oldham-Cooper and Loades (2017), Higa-McMillan et al. (2016), Silverman et al. (2008), Warwick et al. (2017), and Thulin et al. (2014) providing a comprehensive overview of the randomized controlled trials (RCTs) that tested CBT clinical efficacy and effectiveness focusing specifically on the reduction of SAD symptoms and of SAD diagnosis remission rates, comparing transdiagnostic CBT protocols against disorder-specific ones in different age targets, whereas previous reviews were focused on generic anxiety disorders without providing any indications about for whom and for what extent specific formats of CBT were more efficacious in addressing separation anxiety. Our findings suggest that disorder-specific CBT protocols, which encounter the active inclusion of caregivers within the therapeutic process, are necessary for producing optimal outcome measures among pre-schoolers, while transdiagnostic CBT protocols are preferred with school-aged children and adolescents. Anxiety runs in families (Battaglia et al., 1995; Burstein et al., 2010; Eley et al., 2015; Scaini et al., 2012; Xu et al., 2020), and parents with anxiety disorders may involuntarily elicit anxiety in their children through reinforcement and modelling (Barrett et al., 1996a, b; Burstein & Ginsburg, 2010; Drake & Ginsburg, 2012; Fisak & Grillis-Taquechel, 2007). Cobham et al. (1998) reported that children with anxious parents benefited more from CBT that included tailored parent-sessions than from

individual CBT, whereas children of non-anxious parents benefited from both treatments. Mixed results regarding the role of parental involvement in CBT have been found in previous meta-analyses (Dorsey et al., 2017; Thulin et al., 2014; Weersing et al., 2017), whereas this review offered support to the notion that parent–child CBT interventions result in greater symptoms reduction and diagnosis remission rates among preschoolers than school-aged children and adolescents. Some forms of parent training may be particularly useful for parents of SAD pre-schoolers to teach them more adaptive coping strategies and to enhance awareness about their dysfunctional parental style toward children which might act as a maintenance factor of the disorder. Parents might limit adaptive exploration of the surroundings by fomenting a sense of pathological dependence on the caregiver, seen as necessary to face life’s challenges (Bögels & Siqueland, 2006; Cobham et al., 1998; Thienemann et al., 2006). The differential efficacy of parental involvement among different age targets might be interpreted as a consequence of the extent to which children and adolescents rely on their parents to get strategies for coping with distress.

It is interesting to note that CBT showed to be an effective, structured, problem-oriented psychotherapeutic approach aimed at modifying not only dysfunctional behavioral patterns, using extinction programs that are rooted in learning theories, but also how the subject selects and processes information to enhance emotional well-being and adaptation to the environment (D’eramo & Francis, 2004). Our findings also showed that CBT boasts higher relative effectiveness than drug treatment either in the short or long term (Piacentini et al., 2014; Walkup et al., 2008). The use of drugs in childhood is not considered as the first-choice therapy for the treatment of mental disorders, especially in the face of studies that validate the efficacy of psychotherapeutic intervention protocols, such as CBT, in its different formats (Almqvist et al., 2005; James et al., 2005, 2013; Silverman et al., 2008). Drugs act on a symptom level but leave underlying dysfunctional cognitions untreated. This is dangerous, as pervasiveness and persistence of dysfunctional cognitions represent the main causes of relapse as soon as the drug treatment is suspended.

Furthermore, both individual and group CBT proved to be effective in addressing the core symptoms and related impairments of SAD, with no overall significant differences between them, lending support to the efficacy and effectiveness of both formats of delivery in schoolers and adolescents (Kodal et al., 2018; Villabø et al., 2018; Wergeland et al., 2014). These findings confirmed that of Sigurvinsdóttir and colleagues’ review (2020).

One of the major limitations for a consistent interpretation of these results was the wide clinical heterogeneity that has been encountered across the reviewed studies, as patients, whose age varies within a broad range, often fulfil diagnostic criteria for more than a single anxiety disorder. Moreover, some studies have considered as main outcome measure whether the child was free of the primary and most interfering anxiety disorder while in others it reflected whether the child was free of all anxiety disorder diagnoses, and instruments administered were only partially comparable. Another important limitation dealt with the assessment of CBT clinical efficacy, which was mainly based on categorical outcome measures, whereas evaluations of functional outcomes, such as improvements in life quality, interpersonal relationship, and family dynamics, were excluded by most studies. Moreover, future

longitudinal studies should explore the course of SAD throughout follow-ups that are not limited to the first years after the end of treatment and should include the assessment of socio-demographic and individual variables. A growing body of literature (Barrett et al., 2001; Ginsburg et al., 2014; Kendall & Southam-Gerow, 1996; Kendall et al., 2004; Saavedra et al., 2010) has pointed out the maintenance of CBT treatment gains up to 19 years of follow-ups (Benjamin et al., 2013), suggesting important durable clinical benefits of successful early CBT for anxious children and adolescents. However, all the abovementioned studies relied on a transdiagnostic CBT protocol administered to widely heterogeneous samples, either in terms of primary diagnosis or age. Information about the long-term efficacy of disorder-specific CBT protocols for SAD is required to provide evidence about the necessity of early interventions to reduce the sequelae of childhood anxiety disorders, if left untreated, especially for pre-schoolers. Notably, except for the study of Kodal et al. (2018), little is known about the therapeutic outcomes 3 or 4 years or even more after the end of the treatment. Additionally, the study of Kodal et al. (2018) is characterized by the lack of a control group. This methodological limitation does not allow causal associations between treatment and therapeutic outcome, because it is not possible to exclude spontaneous remission or maturational effects as potential contributing factors.

Future research should carry out analyses aimed at finding potential predictors and moderators of the final therapeutic goals, such as the severity of symptoms, comorbid disorders, duration of therapy, type of CBT protocol, emotional distress in parents, and maladaptive anxiety regulation strategies. As suggested by Cobham et al. (1998), one of the most robust moderators of the child treatment outcome is a maternal anxiety disorder. Children with non-anxious mothers are more likely to be free of their primary anxiety diagnosis at follow-up, compared with children with anxious mothers, supporting the existence of a reciprocal relationship between parental and child anxiety. Nevertheless, the role of further moderators and predictors of treatment outcome should be investigated. In this regard, the identification of profiles of children responding to specific treatments would allow a more prescriptive selection of patients for target age-related clinical interventions.

Conclusion

The current review supports the efficacy and effectiveness of different CBT formats in reducing the severity of SAD symptoms and in fostering a significant remission of SAD diagnosis among children and adolescents with specific considerations to age ranges. CBT is a time-limited and skills-building approach that addresses the core symptoms of the pathology in an effective, fast, and goal-directed way, modifying dysfunctional behavioral patterns and cognitive beliefs also in younger children. Findings show that CBT is significantly associated with remission diagnosis and reduction of symptom severity when offered as a child-focused treatment or in combination with sertraline, especially among school-aged children and adolescents. However, relevant outcome measures were obtained also when offered as family-based disorder-specific psychotherapy, but targeted interventions on parental

maintenance factors for SAD added larger therapeutic benefits on child-based CBT mainly among pre-schoolers and younger children. As a future clinical implication, these findings could offer mental health professionals the opportunity to access an increasingly greater number of therapies with emerging empirical support, whose choice is strictly related to the main features of the patient's psychopathological profile.

Author Contribution LG and SS independently inspected and screened all full-text articles identified by the search that met eligibility criteria for inclusion in the review. LG wrote the manuscript and MC, BF, GM, and SS critically reviewed the first draft contributing to the discussion. All authors approved the final version of the manuscript.

Declarations

Ethics Approval No ethical approval was required for this work.

Conflict of Interest The authors declare no competing interests.

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