Child Psychiatry & Human Development (2020) 51:209–219
https://doi.org/10.1007/s10578-019-00923-3

ORIGINAL ARTICLE

A Pilot Study of Family-Based Exposure-Focused Treatment for Youth with Autism Spectrum Disorder and Anxiety

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Published online: 6 September 2019

Abstract

Anxiety is a common and impairing condition in youth with autism spectrum disorders (ASD). Evidence supports the use of cognitive behavioral therapy for treating anxiety in this population; however, available treatment protocols may be difficult to implement outside of research settings. The present study examined the efficacy of family-based exposure-focused treatment (FET) compared to a treatment as usual (TAU) control in 32 youth aged 6–17 years with ASD and co-occurring anxiety. Fourteen youth were randomized to FET, which included 12 face-to-face weekly therapy sessions lasing 45–55 min, while 18 youth completed the TAU control where engagement in psychotherapy or pharmacotherapy was at the discretion of the families. Results strongly supported FET with a 79% (versus 0% in TAU) response rate, 86% (versus 0% in TAU) remission in primary anxiety diagnosis, and large between-group effects on clinician-rated anxiety severity and most parent-rated domains of anxiety-related impairment. Among treatment responders, 2-month follow-up supported maintenance of gains. Overall, the study supported FET as a relatively brief intervention for the treatment of anxiety in youth with ASD, although further research is needed to replicate these findings and compare FET outcomes to more comprehensive interventions.

Keywords Anxiety · Autism spectrum disorders · Children · Exposure therapy · Family-based treatment

Introduction

Autism spectrum disorders (ASD) are a neurodevelopmental disability with core features including deficits in social communication/interaction and patterns of restrictive or repetitive behaviors/interests [1]. Youth with ASD experience difficulty with social reciprocity, predisposing this population to a wide range of social/relational impairments [2]. Anxiety disorders are among the most commonly reported comorbidities for youth with ASD [3]; prevalence estimates range from 40 to 55% for at least one co-occurring anxiety disorder, although rates as high as 84% have been reported [4–7]. Specific diagnoses observed in this population include specific phobias (30–44%), social anxiety disorder (17–30%), obsessive–compulsive disorder (OCD; 17–30%), generalized anxiety disorder (GAD; 15–35%), and separation anxiety (9–38%), and many youth meet criteria for more than one anxiety disorder [7, 8]. There are many possible explanations for the wide variability in reported rates, including inconsistent assessment methodologies, atypical symptom presentation, symptom overlap, and diagnostic overshadowing [9–11]. Regardless, anxiety disorders are more common

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among youth with ASD than in the general population [8, 12–16].

Consistent with the elevated prevalence of anxiety disorders in youth with ASD, parents rate anxiety as the second most common problem [17, 18]. Further, symptoms of anxiety often motivate parents of youth with ASD to seek treatment [8, 12–16]. Anxiety can exacerbate core features of ASD, such as over-responsivity to sensory stimuli [19–22] and contribute to heightened social deficits [23], depressive symptoms [24], and family/peer relationship difficulties [25]. The presence of an anxiety disorder results in functional impairment over and above that related to ASD alone, affecting multiple domains including quality of life, employment, and educational attainment [17, 24, 26–28]. Untreated anxiety symptoms are generally stable in individuals with ASD, and untreated anxiety may persist into adulthood [29, 30]. Given the wide-ranging and potentially long-term impact of anxiety disorders on youth with ASD, identifying and disseminating efficacious treatments to target anxiety in this population—as well as understanding core interventional components—is of great importance.

In typically developing populations, both behaviorally oriented psychosocial (i.e., cognitive behavioral therapy [CBT]) and pharmacological (i.e., selective serotonin reuptake inhibitors [SSRIs]) interventions have been established as first-line treatments for youth anxiety [31, 32]. However, there is a relatively limited number of randomized clinical trials investigating the treatment of anxiety among youth with ASD [33, 34]. Currently, there is insufficient evidence to recommend SSRI treatment for anxiety in youth with ASD, especially given the potential for SSRI-related side effects [35]. Parents report an overwhelming preference for behavioral treatment [34, 36], which has been established by multiple randomized trials as an empirically supported treatment for anxiety in youth with ASD [28, 37].

Of the available CBT protocols for youth with ASD and comorbid anxiety, one of the best-studied is behavioral interventions for anxiety in children with autism (BIACA), a family-based CBT protocol developed by Wood et al. [38] consisting of 90 min sessions delivered over 16 weeks. In a pilot randomized trial of 40 youth with ASD and anxiety, 78% of youth receiving BIACA responded to treatment compared with 9% in the waitlist control group [38]. Storch et al. [39] replicated this finding in a randomized trial of 45 youth (ages 7–11) and found a response rate of 75% for those receiving CBT, as compared to 14% receiving treatment-as-usual (TAU) [38]. Wood et al. [40] randomized 33 adolescents (ages 11–15) and found a 79% response rate in favor of BIACA compared to 29% in the waitlist control. Likewise, a later study by Storch et al. [41] randomized 31 youth (ages 11–16) to CBT or TAU and found a 69% response rate for BIACA compared to 27% in the TAU group. Additionally, a 3 year multisite randomized controlled trial is underway, investigating the efficacy of BIACA as compared to an active control [42]. A strength of BIACA is that, in addition to anxiety-focused cognitive behavioral content (e.g., responding to anxious thinking, fear hierarchy development, and exposure), the protocol also includes modules on several related skills relevant to youth with ASD (i.e., rewards/consequences, social skills, fixated interests, friendships, and mentoring).

Despite the promising evidence of treatment efficacy in children and adolescents, use of BIACA in non-research settings may be limited by the time-intensive nature of the intervention. The protocol entails sixteen sessions, each up to 90 min in length, and extensive therapist training is required. Importantly, due to changes in standards for reimbursement from third-party payers, sessions lasting longer than 60 min are no longer covered [43]. Additionally, many managed care companies do not cover sessions longer than 45 min and place stipulations on the number of sessions covered in a calendar year [43]. Finally, the extent to which exposure-therapy is a core treatment component requires examination, given that the trajectory towards improvement in BIACA appears to begin with the introduction of exposure [44, 45]. Similar findings have been observed in non-ASD populations, with anxiety improvement during CBT accelerated by the introduction of specific CBT skills; cognitive restructuring and exposure [46]. Accordingly, developing a streamlined, accessible intervention for youth with ASD and anxiety is crucial to improving accessibility of treatment.

In response to the need for modified treatments, we developed a new treatment protocol of family-based exposure focused treatment (family-based exposure-focused treatment; FET) for youth with ASD and co-occurring anxiety. Developed based on the promising BIACA findings [38–41] as well as the broader clinical literature for childhood anxiety and OCD that embraces family-based exposure therapy [47–49], the FET protocol emphasizes family-focused sessions and exposure. Extant evidence suggests that a family-based, exposure-focused approach may be the most effective method to treat anxiety for youth with ASD [50]. For example, modifying treatment to fit the needs of youth with ASD (i.e., reducing affective and cognitive elements, placing emphasis on tangible behavioral components) and involving the family system in every session may allow these youth to benefit from treatment despite inherent difficulties associated with ASD [51, 52], and may be particularly important for treating younger children with anxiety [53]. Furthermore, this approach could allow this to be done without significant tailoring or modification. Instead of the two 45 min blocks per session in BIACA (i.e., a child session and a separate parent session), FET incorporated teaching, skills practice, and problem solving with parent(s) and child together. With the goal of broadening accessibility and feasibility, FET is streamlined to focus on anxiety using family-based exposure

therapy which is highly acceptable to parents [54]. As a result, use of this approach could reduce the need for specialized training and facilitate dissemination to improve access to evidence-based treatment for youth with ASD and anxiety. Although not yet examined in youth with ASD and anxiety, family-based, exposure-focused approaches have been utilized to modify treatment for other populations, such as reducing the developmental demands of treatment for young children with OCD [48, 54]. Additionally, exposure has been a core component related to symptom improvement of many previously examined treatment protocols [46].

The aim of the present study is to examine the preliminary efficacy of a pilot study of FET for youth with ASD and co-occurring anxiety. Specifically, the study aimed to (1) examine rates of symptom reduction and diagnostic remission in comparison to a TAU control, (2) evaluate changes in parent-reported impairment as well as anxiety and ASD related symptomology following FET or TAU, and (3) examine the short-term stability of gains among treatment responders.

Methods

Participants

Forty children and adolescents between the ages of 6–17 years ($M = 10.03$ years, $SD = 2.81$), along with their parents participated in this study which began July 2012 and concluded May 2015. A broad age range was included to maximize the translational potential of FET and given evidence that exposure therapy is useful across the age span [3]. All enrolled participants had to meet the following inclusion criteria: (1) DSM-IV-TR diagnostic criteria for an autism spectrum disorder as determined by the Autism Diagnostic Observation Scale [ADOS; 55] and the Autism Diagnostic Interview-Revised [ADI-R; 56]; (2) clinical severity rating of ≥ 4 of a primary anxiety disorder as determined by the Anxiety Disorder Interview Schedule-IV Child and Parent Interview Schedules [ADIS-IV-C/P; 57]; (3) a score of ≥ 12 on the Pediatric Anxiety Rating Scale [PARS; 58]; and (4) an IQ score of ≥ 70 as assessed by the Wechsler Abbreviated Scale of Intelligence [WASI; 59][1] Participants were excluded if they were (1) actively suicidal; (2) had a lifetime diagnosis of bipolar disorder, schizophrenia, schizoaffective disorder, or substance abuse; or (3) had a recent change in psychotropic medication. Of the 40 participants assessed, 32 were found suitable for participation and randomized. See Fig. 1 for a CONSORT diagram of enrollment, allocation, treatment, and assessment activities.

Procedure

Local Institutional Review Board (IRB) approval was obtained prior to the study. All assessment and treatment sessions were provided by doctoral level clinical psychology students or fellows with more than 1 year of experience providing CBT for pediatric anxiety disorders, located at a tertiary care clinic specializing in pediatric obsessive compulsive and anxiety disorders. Therapists received individual supervision between treatment sessions from a licensed psychologist. Prior to any testing, written informed consent was obtained from the participant's legal guardian and written assent from the child. After consenting, participants attended a two-part in-person screening assessment conducted by a trained doctoral student independent evaluator (IE). The main purpose of this assessment was to determine whether a participant met eligibility criteria and to establish a baseline symptom level. Participants who met eligibility criteria were randomized in a 1:1 ratio to receive either FET or TAU. Youth randomized to TAU were offered FET after treatment. Upon completion of their respective treatment condition, families completed a post-treatment assessment that was identical to the screening assessment. Treatment responders were classified as those who showed "much to very much improvement" as measured by the Clinical Global Improvement scale (see Measures section below) during the post-treatment assessment. Those in the FET arm who were identified as treatment responders participated in a 2 month follow-up assessment. Following the post assessment, non-responders to TAU were given the option to engage in 12 sessions of FET. All clinician-rated measures were administered by supervised IEs blind to the treatment conditions blind to the treatment conditions at all assessment points. Regular clinical supervision was held to maintain measurement fidelity. A certified faculty member administered the ADOS/ADI-R.

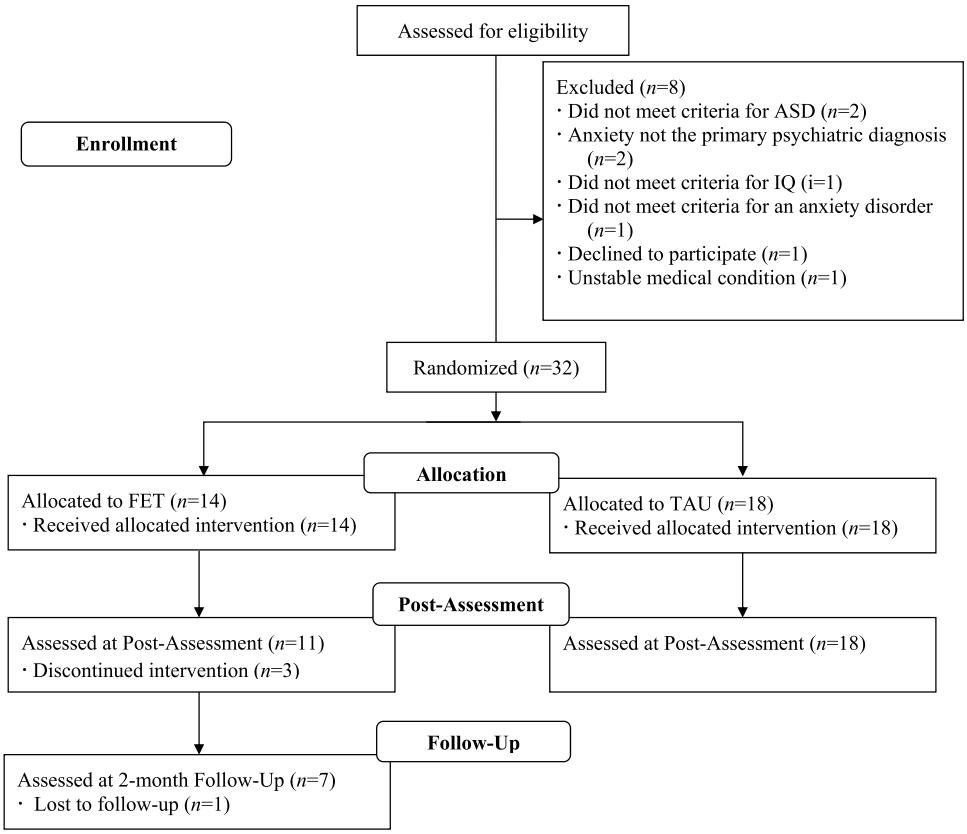
Treatment

FET

Participants assigned to the FET condition engaged in 12 face-to-face weekly therapy sessions. Each session lasted between 45–55 min with both parent and child present. The content covered during the therapy sessions consisted of psychoeducation and hierarchy development (Session 1), reward systems (Session 2), and exposure (Session 3–12). An optional session to address problematic oppositional behavior could be utilized if behavioral challenges that prevented the successful completion of treatment emerged.

[1] Data were collected before use of the ADOS-2 and WASI-II.

Fig. 1 Consort diagram



Therapists were provided a manual outlining each of the aforementioned core elements with language specifically adapted for children and adolescents with ASD.

FET includes ASD-focused modifications related to anxiety-focused elements (e.g., tailored language, emphasis on rewards). Parents are involved in the entire session with the aim of teaching parents to serve as social support/coaches for exposure, enhance motivation and generalization, and reduce accommodation of anxiety [54]. Additionally, parents find this approach highly acceptable [54]. The protocol does not include any additional sessions focused on other ASD-related domains (e.g., functional communication, socialization, stereotyped interest/behavior, adaptive skills/functioning).

TAU

Participants assigned to TAU were allowed to initiate, change, or not engage in any form of psychotherapy or pharmacotherapy for 12 weeks; this decision was at the discretion of the families. Interested families were given information about treatment providers in the community who provided evidence-based services (e.g., CBT). The Service Assessment for Children and Adolescents-Service Use Scale [60] was used to determine whether any mental health services were sought during the TAU 12-week period. Of the 18 TAU participants, the majority (n = 16, 88.9%) received either treatment, medication management, assessment, or special educational support. Of the 13 (72.2%) participants who received treatment services during the study period, 8 (44.4%) received individual treatment, 6 (33.3%) received group treatment, and 7 (38.9%) received treatment at school. Other common services were assessments e.g. psychologists, speech therapists, and occupational therapists (n = 8, 44.4%), medication management (n = 8, 44.4%), and special educational support (n = 6, 33.3%). Utilization of clinical services (mental health professional, pediatrician or family doctor, or emergency room treatment) varied from 0 to 120 h (Median 11, IQR 0.0–25.9 h). Non-responders to TAU at post treatment (n = 18, 100%) were offered access to FET.

Baseline Measures

Autism Diagnostic Observation Scale (ADOS)

The ADOS is a semi-structured diagnostic interview used to assess communication, social interaction, play, and restricted and repetitive behaviors, with behaviors and responses coded by the clinician [55]. Specific cut-off scores vary depending on the module administered, but all modules provide a classification of autism, autism spectrum, or non-spectrum.

Autism Diagnostic Interview-Revised (ADIR)

The ADIR is a structured interview used for diagnosing autism and distinguishing autism from other developmental disabilities [56]. A trained clinician administers the interview to a parent or caretaker who has information on the developmental and current functioning of the person being assessed. There are 93 questions across three domains; language/communication, reciprocal social interactions, and restricted repetitive and stereotyped behaviors and interests. Categorical results are used rather than norms or scaled scores.

Wechsler Abbreviated Scale of Intelligence (WASI)

The WASI is an individually administered intelligence test for individuals aged 6–89 years [59]. It includes four subtests used to develop a full scale IQ; vocabulary, block design, similarities, and matrix reasoning.

Outcome Measures

Interviewer-Rated Measures

Pediatric Anxiety Rating Scale (PARS) The PARS is a clinician-rated scale used to assess anxiety symptoms and associated severity in children, with parent and child interviewed together [58]. The PARS five-item total scores range from 0 to 25 with each item scored on a 0–5 scale.

Anxiety Disorder Interview Schedule-IV Child and Parent Interview Schedules (ADIS-IV-C/P) The ADIS-IV-C/P is a semi-structured clinician-rated diagnostic interview that measures the presence and severity of anxiety, mood, and externalizing disorders [57]. The interview is conducted with parent and child separately. The severity of the disorders is rated by the therapist based on parent and child report as a clinical severity rating (CSR), which can range from 0 to 8. Scores of ≥ 4 from the therapist indicate the presence of a disorder.

Clinical Global Impression-Severity and Improvement (CGI-S/CGI-I) The CGI-S is a clinician-reported measure that assesses overall severity of anxiety symptomology on a 0 (no symptoms) to 6 (extremely severe symptoms) scale. The CGI-I assesses overall improvement of anxiety symptoms on a 0 (very much worse) to 6 (very much improved) scale [61]. Children given a score of 5 "much improved" or 6 "very much improved" on the CGI-I during the post-treatment assessment were considered treatment responders.

Service Assessment for Children and Adolescents-Service Use Scale (SACA) The SACA is a standardized clinician-rated measure that assesses the use of a broad array of different psychiatric services [60]. The SACA has been used to measure a variety of treatments in numerous pediatric anxiety treatment studies [39, 41, 62].

Parent-Rated Measures

Childhood Anxiety Impact Scale-Parent (CAIS-P)

The CAIS-P is a parent-rated measure that assesses overall impact of anxiety symptoms in several domains of a child's life consisting of 33 items using a 4-point Likert scale [63].

Multidimensional Anxiety Scale Children-Parent (MASC-P)

The MASC-P is a 39-item parent-rated measure of the child's anxiety. This psychometrically-sound measure assesses the presence of anxiety related symptoms by using a 3-point Likert scale [64].

Social Responsiveness Scale (SRS)

The SRS is a 65-item parent-rated measure of the child's overall social functioning across multiple domains [SRS]; [65]. The SRS is scored on a 5-point Likert scale and has good reliability and validity across varying cultures [66].

Child Behavior Checklist (CBCL)

The CBCL is a 113-item parent-report measure of the child's behavioral and emotional functioning [67]. For this study, two broad subscales were used measuring children's internalizing and externalizing symptoms.

Child Sheehan Disability Scale for Parents (CSDS-P)

The CSDS-P is a five-item parent-rated measure assessing the interference of the child's anxiety symptoms in multiple life domains [68]. Each domain's interference is scored on a 0 to 10 scale.

Analytic Plan

Group differences on continuous outcomes were evaluated by ANCOVAs, with post-treatment scores being predicted by treatment group while including pre-treatment scores as a covariate. Group differences for categorical outcomes were evaluated by binomial proportion tests. Symptom change at 2 month follow up was evaluated via paired t tests for continuous outcomes and binomial proportion tests for categorical outcomes. Effect sizes were converted into Cohen's d [69], with values of d of 0.2, 0.5, and 0.8 corresponding to small, medium, and large effect sizes, respectively [70].

Missing data were addressed via PROC MI in SAS 9.4 using predictive mean matching and the fully conditional specification method. Missing data (10.1% of outcome data points) were in the acceptable range for multiply imputed models according to criteria described by Graham [71], and auxiliary covariates were used in imputation models (a process that can take data that are not missing at random and produce estimates that are consistent with those that meet the missing at random assumption [72]. Auxiliary covariates included all time points for the outcome being analyzed as well as treatment group. Because improvement scores are not available at screening, no pre-treatment CGI-I scores were available for imputation, and because all treatment responders were by default in the active treatment condition, treatment group was not used as an imputation variable for analyses involving 2 month follow up. Additionally, 2 month follow-up scores were not used as a covariate in post treatment comparisons. Degrees of freedom for multiple imputed hypothesis testing models were adjusted based on recommendations by Barnard and Rubin [73] and 100 imputations were employed.

Results

Participant Characteristics

Information on participant demographics for the FET and TAU groups are presented in Table 1. The groups did not differ significantly on any of the demographic variables.

Table 1 Participant characteristics by treatment condition

	FET ($n=14$)	TAU ($n=18$)	p[a]
Child mean age	10.07 ($SD=2.89$)	10.00 ($SD=2.83$)	0.945
WASI full-scale IQ	100.1 ($SD=15.8$)	107.7 ($SD=15.6$)	0.191
ASD diagnosis			0.422
Autism	5 (35.7%)	5 (27.8%)	
Asperger's disorder	9 (64.3%)	11 (61.1%)	
PDD-NOS	0 (0.0%)	2 (11.1%)	
Child sex (male)	10 (71%)	16 (88.9%)	0.365
Child ethnicity			0.879
White	11 (79%)	13 (72%)	
African American	1 (7%)	1 (6%)	
Asian	1 (7%)	1 (6%)	
Latino/Hispanic	1 (7%)	3 (17%)	
Primary anxiety disorder			0.977
Social phobia	6 (43%)	7 (39%)	
OCD	2 (14%)	3 (17%)	
GAD	5 (36%)	6 (33%)	
Specific phobia	1 (7%)	2 (11%)	
Comorbid diagnoses			
Social phobia	2 (14%)	5 (28%)	0.426
SAD	3 (21%)	5 (28%)	1.00
OCD	1 (7%)	4 (22%)	0.355
GAD	2 (14%)	7 (39%)	0.235
ADHD	9 (64%)	11 (61%)	1.00
ODD	0 (0%)	4 (22%)	0.113
Specific phobia	8 (57%)	10 (56%)	1.00
Selective mutism	0 (0%)	1 (6%)	1.00
Psychiatric medication use			
SSRI	3 (21%)	2 (11%)	0.326
SNRI	1 (7%)	0 (0%)	0.389
Stimulant	4 (28%)	6 (33%)	1.00
Alpha 2 agonist	2 (14%)	6 (33%)	0.367
Antipsychotic	0 (0%)	2 (11%)	0.497
Analgesic	0 (0%)	1 (6%)	1.00

Abbreviated scale of intelligence

OCD obsessive compulsive disorder, *GAD* generalized anxiety disorder, *SAD* separation anxiety disorder, *ADHD* attention deficit hyperactivity disorder, *ODD* oppositional defiant disorder, *PDD-NOS* pervasive developmental disorder—not otherwise specified, *SSRI* selective serotonin reuptake inhibitor, *SNRI* selective-norepinephrine reuptake inhibitor, *WASI* Wechsler

[a]p value based on independent t test for continuous variables and Fisher's exact test for categorical variables

Post-Treatment Outcomes

Primary Outcomes

Table 2 presents descriptive information and ANCOVA analyses for IE-rated measures. We first evaluated whether participants in the FET group demonstrated greater reductions in anxiety severity than the TAU group. On continuous measures, the FET group reported greater reductions in the primary anxiety severity measures, with large effects observed for the PARS, ADIS-C/P CSR, and CGI-S (see Table 1). On dichotomous measures of remission, FET outperformed TAU both for CGI-I (78.6% vs. 0.0%) and ADIS-CSR (85.7% vs. 0.0%) measures of remission.

Secondary Outcomes

Table 2 also reports ANCOVA analyses for parent-report questionnaires. Compared to the TAU group, FET group membership was associated with large reductions in CAIS-P total scores, school and home subscales, CBCL internalizing symptoms, and SDS-rated interference. Medium sized reductions were also reported for CAIS-P global impact and CBCL Externalizing symptoms. However, no significant group effect was found for change in SRS total score or subscales, MASC-P anxiety symptoms or CAIS-P social anxiety symptoms.

Table 2 Descriptive statistics, inferential statistics, and effect sizes for primary and secondary outcomes at all timepoints

Measure	Baseline		Post-treatment				2-month follow up		
	FET *M* (*SD*)	TAU *M* (*SD*)	FET *M* (*SD*)	TAU *M* (*SD*)	t[b]	*d*[b]	FET *M* (*SD*)	*t*[c]	*d*[c]
IE-rated									
PARS	14.07 (2.34)	16.22 (2.67)	7.79 (5.37)	15.06 (3.21)	3.47**	1.01	3.58 (4.28)	0.93	0.35
ADIS CSR[a]	4.50 (0.52)	5.33 (0.84)	2.05 (1.85)	5.00 (0.77)	3.88**	1.11	0.43 (0.77)	2.28	0.82
CGI-S	3.29 (0.73)	3.67 (0.59)	2.25 (0.87)	3.67 (0.69)	4.45**	1.22	1.42 (0.52)	1.26	0.46
Parent-rated									
CAIS-P									
Total	33.90 (16.89)	29.58 (15.23)	16.49 (14.95)	32.10 (16.11)	3.18**	1.04	12.48 (16.28)	−0.53	−0.20
School	14.01 (6.64)	11.71 (6.58)	4.59 (4.09)	13.29 (6.44)	4.92**	1.71	5.56 (7.83)	−0.71	−0.26
Social	9.98 (7.01)	8.19 (6.80)	5.53 (5.90)	8.58 (6.65)	1.97	0.58	2.77 (3.09)	0.23	0.10
Home	4.79 (3.51)	6.01 (4.56)	2.21 (2.72)	5.72 (3.77)	2.59*	0.81	2.36 (6.04)	−0.62	−0.22
Global	6.36 (1.91)	6.49 (2.53)	3.52 (3.20)	6.00 (2.51)	2.52*	0.75	0.96 (0.98)	1.36	0.49
MASC-P	45.74 (13.13)	50.82 (13.80)	38.59 (15.84)	53.51 (14.82)	1.91	0.54	24.78 (11.41)	1.57	0.65
SRS									
Total	100.07 (24.61)	102.50 (24.21)	84.58 (25.98)	98.56 (24.90)	1.44	0.47	81.21 (26.69)	−0.43	−0.16
Awareness	13.07 (4.14)	11.44 (3.33)	11.22 (3.62)	12.06 (3.78)	1.22	0.39	13.43 (3.92)	−2.64*	−1.03
Cognition	20.14 (4.66)	20.50 (5.84)	16.17 (5.45)	19.06 (5.06)	1.49	0.48	16.22 (6.30)	−0.38	−0.14
Communication	33.57 (8.48)	32.94 (8.29)	29.09 (9.21)	32.67 (8.73)	1.36	0.41	26.39 (8.40)	0.25	0.09
Motivation	16.79 (6.00)	17.72 (6.04)	13.23 (5.27)	15.17 (5.55)	0.86	0.26	12.05 (2.78)	−0.73	−0.27
Mannerisms	16.50 (6.76)	19.89 (6.91)	14.94 (6.92)	19.61 (7.38)	1.41	0.48	13.65 (7.96)	0.05	0.02
CBCL									
Internalizing	13.12 (6.45)	17.74 (6.64)	10.61 (8.20)	20.41 (7.60)	2.55*	0.84	4.88 (4.96)	2.27	0.84
Externalizing	10.00 (8.68)	14.27 (8.62)	5.60 (4.12)	16.99 (12.32)	2.80**	0.79	4.41 (3.31)	1.07	0.43
SDS	22.14 (11.48)	30.00 (11.59)	12.02 (11.96)	26.83 (11.61)	2.62*	0.84	3.34 (4.74)	1.00	0.36

[a]Clinical severity rating associated with principal diagnosis

[b]Post-treatment analyses evaluated the effect of treatment condition while accounting for baseline group differences

[c]Analyses compare 2-month follow-up to post-treatment status for treatment responders

*$p < .05$; **$p < .01$

2-Month Follow Up

Because there were no treatment responders from the TAU group, treatment group was not used as an auxiliary covariate in imputation models for analyses of 2-month follow up data. In considering changes from post-treatment to 2-month follow up, no significant changes in symptoms were observed for analyzed variables at the $p < 0.05$ level, with the exception of an increase in symptoms on the SRS Awareness subscale (see Table 2); however, primary outcomes appeared to demonstrate small-moderate continued improvements from post-treatment ($d = 0.35 - 0.82$). In considering follow up response and remission status, 100% of treatment responders retained treatment responder and symptom remission status on all measures (i.e., the CGI-I, CGI-S, and ADIS-IV-C/P CSR) status at 2-month follow up. No hypothesis tests were possible for categorical outcomes at 2-month follow up. This is because 100% of participants were estimated to show response/remission at 2-month follow up.

Discussion

This study presents the preliminary efficacy of a family-based exposure therapy protocol (FET) relative to TAU for children and adolescents with ASD and clinically significant anxiety. Overall, our findings were fairly consistent with outcomes reported in other studies examining structured and modular CBT approaches for this population [38–41, 74, 75]. Approximately 79% of youth responded to treatment (vs. 0% in TAU) and 85.70% achieved clinical remission on the ADIS-IV-C/P CSR (vs. 0% in TAU). While the response rates are consistent with other trials involving youth with ASD and comorbid anxiety, the higher remission rates was a surprise as other studies have generally found lower remission rates. It is possible that this may reflect significant focus on core anxiety treatment components (i.e., exposure therapy). Alternately, it may be an artifact of the small sample size, or the relatively high functioning and moderate anxiety levels among participants. Thus, results must be interpreted with caution and replicated. Effect sizes were large across

a number of clinician-rated instruments, and most parent-reported impairment and internalizing symptoms. However, future studies should be conducted utilizing other recommended treatments for anxiety, which will allow a stronger comparison than a TAU condition. Further, the literature on CBT treatment of anxiety in ASD is encouraging yet still developing [16, 50]; studies are small, use differing approaches in terms of treatment content and symptom targets, and are likely influenced—given their small sample size—by sample characteristics. Like all studies, this must be taken into account when interpreting and framing these data.

We did not detect improvements in SRS-rated ASD symptoms such as social awareness, cognition and communication in the FET group relative to TAU. Although our exposure-focused therapy protocol appeared to have benefit for anxiety symptoms, core ASD symptoms did not improve with treatment. This is not surprising, given that specific modules that target communication deficits, social/peer functioning, and management of ASD symptomology (e.g., stereotyped interests, repetitive behaviors) were not included in FET. It is unclear whether inclusion of such content may result in a more holistic improvement relative to an exposure therapy only protocol, or potentially result in increased intervention acceptability and the possibility of long-term maintenance of treatment gains. Previous studies of interventions which have placed varying emphasis on both anxiety and ASD symptoms and have achieved varying results on both symptom areas. For example, the BIACA protocol has demonstrated strong reductions in anxiety and some reduction in core ASD symptoms [39] while the Multimodal Anxiety and Social Skill Intervention [76], which placed a stronger emphasis on ASD-related deficits, found significant improvements in those areas but not in anxiety. It may be that having too many treatment components may actually dilute intervention effects on anxiety. Further, a more simplified/focused treatment may be easier for clinicians to implement, after which families could seek out alternative specialized treatment to address ASD symptoms.

Although clinician ratings showed sizable differences, similar to some previous findings [41], significant differences in parent-reported child anxiety on the MASC-Parent were not found despite a moderate effect size. This may reflect limited statistical power given our modest sample size, or the challenges of using anxiety symptom specific measures to assess child anxiety among youth with ASD. Indeed, evidence suggests that anxiety presents differently among those with ASD relative to neurotypical youth [7]; thus, certain symptoms may not be captured by the MASC-Parent. Furthermore, the timeframe for assessment of anxiety symptoms differs for the MASC-Parent (within prior month) relative to the PARS (within the last week), which may not capture changes that occurred over the prior month. We observed improvements in externalizing symptoms, which may be linked to reduction in anxiogenic triggers and behavioral management aspects of the treatment, but nonetheless are more directly observable than internalized, anxiety symptoms.

These preliminary outcomes, while impressive, need to be considered in light of other findings. Response rates were similar to other studies [38, 41, 74] that included multicomponent models. When examining the amount of exposure, it was essentially the same as in those studies. The unidimensional focus of the FET model may result in better uptake or understanding of the approach. Notably, our continuous measures of anxiety had relatively modest reductions; thus, longer treatment clearly could be beneficial to some youth. This FET did not demonstrate improvements in social communication, which may be where the benefit from a multicomponent model comes from. Our utilization of parents allowed for therapeutic concepts to be implemented outside of session, an issue we clinically have struggled with other treatment models that involved working with the child alone. Furthermore, families find this approach acceptable and it required their commitment, which may result in positive findings. Rigorous quality assurance and supervision procedures were in place. It is important to recognize that our participants were relatively high functioning, younger, and moderately impacted by anxiety.

Several study limitations are acknowledged. First, although TAU is an improvement over waitlist controls the nature of the interventions received are highly variable in their focus, and likely, in their quality. Further, youth randomized to TAU were offered FET after the TAU period for ethical reasons, so it was not possible to conduct a follow-up comparison of FET outcomes compared to TAU. We thus highlight the need for future studies to incorporate active control conditions (e.g., psychotherapy, pharmacotherapy). Second, we studied a modest sample with adequate power for large main effects; however, there was not adequate power to examine treatment mediators and moderators, or smaller effects. Third, we are not clear if this approach may hold differing value for younger versus older youth; this remains to be investigated. Fourth, our sample was relatively high functioning and not characterized by severe anxiety, ASD, or low IQ. It is likely that children with more severe or complicated clinical presentations may require longer, more intense, or multicomponent interventions. Finally, we used a short follow-up interval; determining the long-term impacts of FET and other CBT protocols is of significant interest.

In sum, the primary contribution of this study is to demonstrate the central role of exposure therapy in reducing anxiety symptoms in working with youth with ASD and comorbid anxiety. While contributing information that exposure therapy demonstrates efficacy in addressing anxiety in this population, the lack of a significant

FET group effect for SRS-rated ASD symptoms suggest a continued and central place for more comprehensive, multimodal interventions that address the sequelae of ASD (e.g., social functioning), such as BIACA, more broadly. While reducing anxiety symptoms and associated impairment is a central target in of interventions, enhancing quality of life and, in this case overall functioning, is also of critical import to achieve wellness. FET may represent a potential alternative to broader treatment programs: it requires visits of reasonable length and duration, necessitates a less intensive training than other interventions, is exposure based and engages family, is similar to treatment of anxiety in neurotypical populations, and is consistent with managed-care intervention models. However, further evaluation is needed. For some youth (perhaps those with less ASD-related impairment or those whose anxiety is the primary domain of interference), this focused program may be an appropriate alternative or could be used as one portion of a segmented treatment plan (e.g., youth separately participates in social skills programming). In sum, this study suggests preliminary support for an exposure therapy based, family focused treatment protocol that may more feasible to implement than alternative interventions.

Summary

This study supports the preliminary efficacy of a relatively brief, family-based exposure-focused treatment (FET) approach for anxiety in youth with ASD. FET was developed as a focused treatment, given insurance constraints and the usual number of sessions that families attend. Potential benefits of the FET approach include comparable simplicity of the protocol (reducing need for any significant therapist training), compatibility with 45–55 min sessions, and adaptability for a wide range of anxiety concerns. Data suggests that FET is associated with significant anxiety reductions and a high rate of treatment response, as determined by independent evaluator interview ratings, and by parent self-report measures. However, sample characteristics must be considered and ultimately replication is needed. FET-related anxiety gains were maintained two-month post treatment. However, FET was not associated with significant reductions in ASD symptoms, indicating that treatments like BIACA may be more useful in simultaneously addressing ASD-related symptoms. Replication is needed with a larger sample and active control condition. Overall, youth with ASD and comorbid anxiety appear to benefit from FET in this small study, which focused on the core elements of CBT for anxiety.

Compliance with Ethical Standards

Conflict of interest Dr. Storch receives grant funding from NIH, Red Cross, Houston Greater Community Foundation, Rebuild Texas, and Texas Higher Education Coordinating Board. He is a consultant for Levo Pharmaceuticals. He receives book royalties from Elsevier, APA, Lawrence Erlbaum, Springer, Wiley, Jessica Kingsley and Oxford University Press. Sophie Schneider has received funding from the Texas Higher Education Coordinating Board and the American Red Cross. Dr. De Nadai receives funding from the Henderson-Wessendorff Foundation. Dr. Selles has received research support from the BC Children's Hospital Research Institute, Michael Smith Foundation for Health Research, speaking honoraria from The AnxietyNZ Trust, and is on the Scientific Advisory Committee for AnxietyCanada. Dr. Lewin receives grant funding from CDC and All Children's Hospital Research Foundation. He receives book royalties from Springer and Jessica Kingsley. Ms. Bergez, Grebe, Ramirez have no conflicts of interest to disclose.

Ethical Approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed Consent Informed consent was obtained from all adult participants included in the study and assent was obtained from all child participants.

Research Involving Animal Participants This article does not contain any studies with animals performed by any of the authors.

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