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Cognitive Behavioral Treatments for Anxiety in Children With Autism Spectrum Disorder
A Randomized Clinical Trial

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IMPORTANCE Anxiety is common among youth with autism spectrum disorder (ASD), often interfering with adaptive functioning. Psychological therapies are commonly used to treat school-aged youth with ASD; their efficacy has not been established.

OBJECTIVE To compare the relative efficacy of 2 cognitive behavioral therapy (CBT) programs and treatment as usual (TAU) to assess treatment outcomes on maladaptive and interfering anxiety in children with ASD. The secondary objectives were to assess treatment outcomes on positive response, ASD symptom severity, and anxiety-associated adaptive functioning.

DESIGN, SETTING, AND PARTICIPANTS This randomized clinical trial began recruitment in April 2014 at 3 universities in US cities. A volunteer sample of children (7-13 years) with ASD and maladaptive and interfering anxiety was randomized to standard-of-practice CBT, CBT adapted for ASD, or TAU. Independent evaluators were blinded to groupings. Data were collected through January 2017 and analyzed from December 2018 to February 2019.

INTERVENTIONS The main features of standard-of-practice CBT were affect recognition, reappraisal, modeling/rehearsal, in vivo exposure tasks, and reinforcement. The CBT intervention adapted for ASD was similar but also addressed social communication and self-regulation challenges with perspective-taking training and behavior-analytic techniques.

MAIN OUTCOMES AND MEASURES The primary outcome measure per a priori hypotheses was the Pediatric Anxiety Rating Scale. Secondary outcomes included treatment response on the Clinical Global Impressions–Improvement scale and checklist measures.

RESULTS Of 214 children initially enrolled, 167 were randomized, 145 completed treatment, and 22 discontinued participation. Those who were not randomized failed to meet eligibility criteria (eg, confirmed ASD). There was no significant difference in discontinuation rates across conditions. Randomized children had a mean (SD) age of 9.9 (1.8) years; 34 were female (20.5%). The CBT program adapted for ASD outperformed standard-of-practice CBT (mean [SD] Pediatric Anxiety Rating Scale score, 2.13 [0.91] [95% CI, 1.91-2.36] vs 2.43 [0.70] [95% CI, 2.25-2.62]; $P = .04$) and TAU (2.93 [0.59] [95% CI, 2.63-3.22]; $P < .001$). The CBT adapted for ASD also outperformed standard-of-practice CBT and TAU on parent-reported scales of internalizing symptoms (estimated group mean differences: adapted vs standard-of-practice CBT, −0.097 [95% CI, −0.172 to −0.023], $P = .01$; adapted CBT vs TAU, −0.126 [95% CI, −0.243 to −0.010]; $P = .04$), ASD-associated social-communication symptoms (estimated group mean difference: adapted vs standard-of-practice CBT, −0.115 [95% CI, −0223 to −0.007]; $P = .04$; adapted CBT vs TAU: −0.235 [95% CI,−0.406 to −0.065]; $P = .01$); and anxiety-associated social functioning (estimated group mean difference: adapted vs standard-of-practice CBT, −0.160 [95% CI, −0.307 to −0.013]; $P = .04$; adapted CBT vs TAU: −0.284 [95% CI, −0.515 to −0.053]; $P = .02$). Both CBT conditions achieved higher rates of positive treatment response than TAU (BIACA, 61 of 66 [92.4%]; Coping Cat, 47 of 58 [81.0%]; TAU, 2 of 18 [11.1%]; $P < .001$ for each comparison).

CONCLUSIONS AND RELEVANCE In this study, CBT was efficacious for children with ASD and interfering anxiety, and an adapted CBT approach showed additional advantages. It is recommended that clinicians providing psychological treatments to school-aged children with ASD consider developing CBT expertise.

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Supplemental content

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Autism spectrum disorder (ASD) affects about 1 of 59 school-aged youth in the United States.[1] Maladaptive and interfering anxiety is common among youth with ASD and associated with functional impairment above and beyond the presence of ASD.[2] In addition to common childhood fears (eg, separation, generalized anxiety), maladaptive distinctive fears (eg, fears of beards, specific sounds, minor change) are also common.[3,4] Higher levels of child anxiety are associated with greater difficulties with school adjustment, social skills, friendship, loneliness, self-injurious behavior, and family conflict in youth with and without ASD.[5-8]

Studies of youth with ASD in the United States have estimated that psychological therapy (often referred to as *psychotherapy*) is among the most frequently used mental health services for youth with ASD, with as many as 23% to 43% of youth accessing this type of treatment.[9,10] Several small randomized clinical trials using wait-list or usual-care control conditions suggest that a specific form of psychotherapy, cognitive behavioral therapy (CBT), may be beneficial for school-aged youth with ASD and anxiety.[11-18] However, no psychological or pharmacological treatments for anxiety in school-aged children with ASD meet contemporary evidentiary standards[19] as efficacious or well-established.

Several CBT programs have been adapted for the characteristics of ASD.[11-15] The rationale for adapted CBT programs for youth with ASD is multifaceted: (1) achieving generalizable symptom change in youth with ASD has been a challenge in some treatment programs,[20] (2) contextual factors that cause anxiety (eg, social communication challenges, ASD-associated stressors) likely necessitate a psychological treatment that addresses these contextual factors,[14] and (3) youth with ASD may benefit from more parental involvement in psychological treatment than is typical in standard-of-practice CBT.[21] Other CBT programs have been developed for typically developing youth but also tested for youth with ASD.[16,17] These initial studies suggest that CBT is a promising modality for treating anxiety in youth with ASD, but study limitations (eg, small samples, use of wait-list control arms) preclude efficacy conclusions.[18] It is unknown whether adapted CBT differs from standard-of-practice CBT in its effects on youth outcomes.

The present study evaluated the efficacy of 2 versions of CBT (adapted CBT and standard-of-practice CBT) for anxiety in youth with ASD using a study design capable of testing relative treatment efficacy with sufficient statistical power, and assessed the effect of CBT on anxiety symptoms, ASD symptom severity, and adaptive functioning. It was hypothesized that (1) children randomized to CBT would exhibit greater improvement in these domains relative to children randomized to treatment as usual (TAU) and (2) CBT adapted for youth with ASD would show advantages over standard-of-practice CBT.

Key Points

Question Does cognitive behavioral therapy (CBT) reduce anxiety symptoms in children with autism spectrum disorder (ASD) and maladaptive and interfering anxiety?

Findings In this randomized clinical trial of 167 children with ASD and maladaptive and interfering anxiety, 2 variants of CBT were compared with a treatment-as-usual condition. Cognitive behavioral therapy designed for children with ASD yielded significantly lower anxiety scores on the primary outcome measure than standard-of-practice CBT and treatment as usual; both types of CBT yielded higher rates of positive treatment response than treatment as usual.

Meaning Per this analysis, CBT is efficacious for the treatment of maladaptive and interfering anxiety in children with ASD.

Methods

The study protocol is included in Supplement 1 and has been summarized elsewhere.[22] Details about the sample and a brief description of the measures, eligibility criteria, and treatment conditions are presented. The Consolidated Standards of Reporting Trials guidelines were followed.

Participants

Participants were a volunteer sample of children with ASD and maladaptive and interfering anxiety; the eligible age range was 7 to 13 years. Three universities in major US metropolitan areas (Los Angeles, California; Tampa, Florida; and Philadelphia, Pennsylvania) served as data collection sites. A power analysis was conducted to determine target sample size.[22]

This study was approved by university-based institutional review boards at each site (University of California, Los Angeles general institutional review board, University of South Florida institutional review board, and Temple University's Human Research Protection Program). Parents gave written informed consent and children gave assent to participate after receiving a complete description of the study.

Telephone contact was initiated by parents to the study coordinator, and an initial screening was conducted. Families received $75 for participating in the assessments. Recruitment began April 2014, and final data were collected in January 2017, coinciding with the grant support period.

Eligibility criteria included having a clinical diagnosis of ASD confirmed by the study's clinical research evaluation, an IQ of 70 or more points (±SEM), and anxiety (as defined by a Pediatric Anxiety Rating Scale [PARS] total score of ≥14 points, which corresponds with maladaptive and interfering anxiety)[23,24] (complete criteria are in the protocol [Supplement 1]). The site principal investigator determined eligibility status at screening. Participants were notified of their eligibility status by the study coordinator and, if eligible, proceeded to complete secondary outcome measures.

Interventions

Participants were randomized using a computer-generated algorithm in a parallel study design with a 4.5:4.5:1 ratio to (1) standard-of-practice CBT (termed *the Coping Cat program*),[25] (2) CBT adapted for ASD (the Behavioral Interventions for Anxiety in Children with Autism [BIACA] program),[14] or (3) TAU. Randomization was conducted by the study statistician (B.J.S.),

who had no contact with participants. The statistician informed the study coordinator of the random assignment for each participant, who subsequently notified participants. Families were not informed of study hypotheses.

Therapists (19 graduate students and postdoctoral fellows) received 8 hours of training in the treatment protocols, read the treatment manuals, and attended weekly supervision sessions with a licensed psychologist. Children were assigned to an available therapist based on availability. The same therapists were trained in and provided both CBT treatments. Both CBT treatments have been described extensively elsewhere[12-15,22,26-29] and in the study protocol (Supplement 1).

Standard-of-Practice CBT

Participants received 16 weekly 60-minute sessions of the Coping Cat program, which was found to be effective in trials of typically developing youth aged 7 to 13 years.[26-29] The main features are (1) recognizing anxious feelings and somatic reactions to anxiety, (2) identifying cognition in anxiety-provoking situations (eg, expectations of threat), (3) developing a plan to cope (eg, reappraisal), (4) imaginal and in vivo exposure tasks, and (5) self-reinforcement for effort. The treatment uses modeling, role-play, and contingent reinforcement. Specific homework tasks are assigned. Parent involvement in the child's treatment includes a regular 15-minute check-in at the start of each session and 2 meetings with the therapist.

Adapted CBT (BIACA)

Like Coping Cat, BIACA uses CBT strategies, such as reappraisal and exposure. The BIACA program differs from Coping Cat in the following ways: (1) children receive 16 weekly 90-minute sessions (split evenly between children and parents) to facilitate parent engagement; (2) BIACA uses a modular format guided by an algorithm to personalize treatment, given the multifaceted clinical presentations in ASD; (3) children's disruptive behavior is addressed as needed with antecedent and incentive-based practices to reduce the influence of aggression and noncompliance on treatment engagement; (4) children are taught social engagement skills as needed (eg, playdate hosting, joining peers at play) to facilitate successful peer-oriented exposure-therapy assignments; (5) the children's special interests are treated as an asset and incorporated into treatment to promote engagement; (6) target behaviors are reinforced with a comprehensive reward system at home and, when relevant, in school to promote motivation and treatment engagement. Further clinical description of BIACA and its treatment algorithm has been published elsewhere.[30-34] An app with training and clinician guidance incorporating the algorithm has been developed for BIACA and associated practices and is available free of charge at https://meya.ucla.edu.

Treatment as Usual

Participants in the TAU arm continued in their usual services and were provided with referrals. No specific treatment recommendations were given. Families were permitted to choose or maintain any treatment approach for 4 months. After TAU, for ethical reasons, families were offered their choice of either CBT condition if their children were still symptomatic.

Therapist Fidelity

Therapists' adherence to the interventions was monitored through session audio recordings. A random selection of sessions (92 for BIACA and 70 for Coping Cat) was coded for fidelity by the principal investigators (P.C.K. and J.J.W.) and trained research assistants. Coders noted the presence or absence of required topics for each session. There was adherence to 97% and 96% of the required topics in BIACA and Coping Cat sessions, respectively. A second coder rated 14.3% of the coded tapes to assess interrater reliability (intraclass correlations: BIACA, 0.85; Coping Cat, 1.00).

Measures

Assessments were conducted by trained, research-certified independent evaluators blinded to treatment condition. Measures were selected based on strong psychometric profiles for youth with ASD. The ASD diagnoses were assigned by an independent evaluator using the Childhood Autism Rating Scale Second Edition–High Functioning Version and the Autism Diagnostic Observation Schedule–2 (ADOS-2). Eligible children met criteria for ASD on algorithm scores from both assessments. A second independent evaluator, unaware of the original scores, independently rated 18 Autism Diagnostic Observation Schedule–2 and 18 Childhood Autism Rating Scale interviews selected randomly, with 100% agreement for meeting ASD criteria on both measures. Each participant's IQ score was assessed using the Wechsler Intelligence Scale for Children–IV; estimated full-scale IQ was based on the Vocabulary and Matrix Reasoning subscales.

The primary outcome measure was the PARS,[35] an independent evaluator–administered scale assessing anxiety symptoms and associated severity and impairment over the past week. The PARS Severity Scale item scores range from 0 to 5 points, with higher scores reflecting more maladaptive and interfering anxiety; a mean of scores on the 7 items was calculated. The PARS, which is psychometrically sound and treatment sensitive in samples of children with ASD,[12-15,36] was administered at baseline, midtreatment (session or week 8), and after treatment (within 1 week of the last session). The median interrater reliability across assessments (r) was 0.88. The Clinical Global Impression–Improvement scale[37] was rated by the independent evaluator after the postbaseline PARS interviews. This scale is a 7-point rating of treatment response ranging from 1 (very much improved) to 7 (very much worse). A rating of 1 or 2 designated a positive treatment response.

Secondary outcome rating-scale measures were completed by parents, including the Child Behavior Checklist, Social Responsiveness Scale–2, and the Child Anxiety Impact Scale (CAIS).[38] Higher scores on all outcome measures reflect more symptoms or impairment; scores are the mean item value of each scale. Secondary outcome measures were administered before and after treatment. Additional detail about these measures is provided in the eMethods in Supplement 2. The Service Assessment for Children and Adolescents[39] was administered to parents after TAU.

Table 1. Demographic and Clinical Characteristics for Behavioral Interventions for Anxiety in Children With Autism (BIACA), Coping Cat, and Treatment-as-Usual Groups[a]

Characteristics	Participants, No./Total No. (%)		
	BIACA Group	Coping Cat Group	Treatment-as-Usual Group
Female children[b]	21/75 (28)	13/72 (18)	0/19
Latino or Latina children[c]	12/63 (19)	15/54 (28)	3/19 (16)
Child's race[c]			
African American/African	7/75 (9)	2/71 (3)	3/19 (16)
Asian/Pacific Islander	6/75 (8)	3/71 (4)	1/19 (5)
White	46/75 (61)	48/71 (68)	11/19 (58)
Native American or Alaskan	2/75 (3)	1/71 (1)	0/19
Multiracial			
African American and white	0/75	2/71 (3)	1/19 (5)
Asian and white	1/75 (1)	0/71	0/19
Unspecified	1/75 (1)	0/71	0/19
Total household income <$40 000	15/72 (21)	13/71 (18)	5/19 (26)
Father's education			
≤High school diploma	14/72 (19)	12/69 (17)	5/17 (29)
≥4-y College degree	40/72 (56)	40/69 (60)	9/17 (53)
Mother's education			
≤High school diploma	6/74 (8)	5/70 (7)	2/19 (11)
≥4-y College degree	47/74 (64)	50/70 (71)	13/19 (68)
Parents currently married	58/75 (77)	52/71 (73)	12/19 (63)
Autism Diagnostic Observation Schedule-2 algorithm total score, mean (SD)	12.92 (3.88)	13.01 (4.09)	12.39 (4.42)
Childhood Autism Rating Scale total score, mean (SD)	34.63 (4.60)	35.63 (4.94)	33.93 (4.12)
Estimated IQ by Wechsler Intelligence Scale for Children-IV, mean (SD)	102.79 (14.56)	101.64 (15.67)	102.35 (14.54)

[a] There was a significant treatment group difference for female children (P = .02). No treatment group differences were significant for any of the other demographic variables. The sample sizes vary within groups, because some demographic data were not provided by some families.

[b] Options for reporting a child's sex were limited to male and female at the time of the study start. Gender identities were not included from the survey, and future research will correct this omission.

[c] Race/ethnicity were queried in the same section of the survey, leading many families to report on race or ethnicity but not both, with limited detail. Future research will include more open-ended questions about race/ethnicity in the surveys.

Protocol Changes

Changes made to the protocol prior to trial onset are detailed in the protocol in Supplement 1. Most importantly, a no-treatment wait-list control condition was initially added; however, because TAU is a more robust comparator than a wait-list control group,[40] it was selected instead. Additionally, during the trial, baseline PARS scores were calculated based on all 7 PARS severity items, instead of 6 of the 7 severity items, as planned at the study onset.[22] As a result, 3 children who were randomized actually had 6-item PARS scores less than the intended inclusion criterion cut score of 14 points; following intent-to-treat principles, these children were included in all analyses. Notably, a cut score of 17.5 on the 7-item PARS has been established as optimal in recent psychometric research[23]; just 2 children in the sample scored at slightly less than this threshold (scores of 17 each).

Statistical Analysis

The primary analyses tested treatment effects using general linear mixed models (GLMMs), with study site as a random effect and the baseline score as a covariate. Deviation effect-coding was used in the GLMMs as an initial omnibus test. All covariates were centered on the grand mean. Significant deviations from the grand mean were further examined in pairwise contrasts among the relevant treatment conditions using dummy coding; significant contrasts are described with Cohen d effect size estimates, calculated as the difference of group means at the end point, using pooled baseline SDs from the full sample as the measure of variability.[41] All GLMMs were estimated using HLM 7.0.1 software (Scientific Software International Inc). Intent-to-treat analyses were conducted by replacing missing values (eg, those attributable to dropout) with multiple imputations using the predictive mean matching method and then testing treatment effects using ordinary least squares regression with the same dummy-coded variables used in the GLMMs. All analyses were by the original assigned groups.

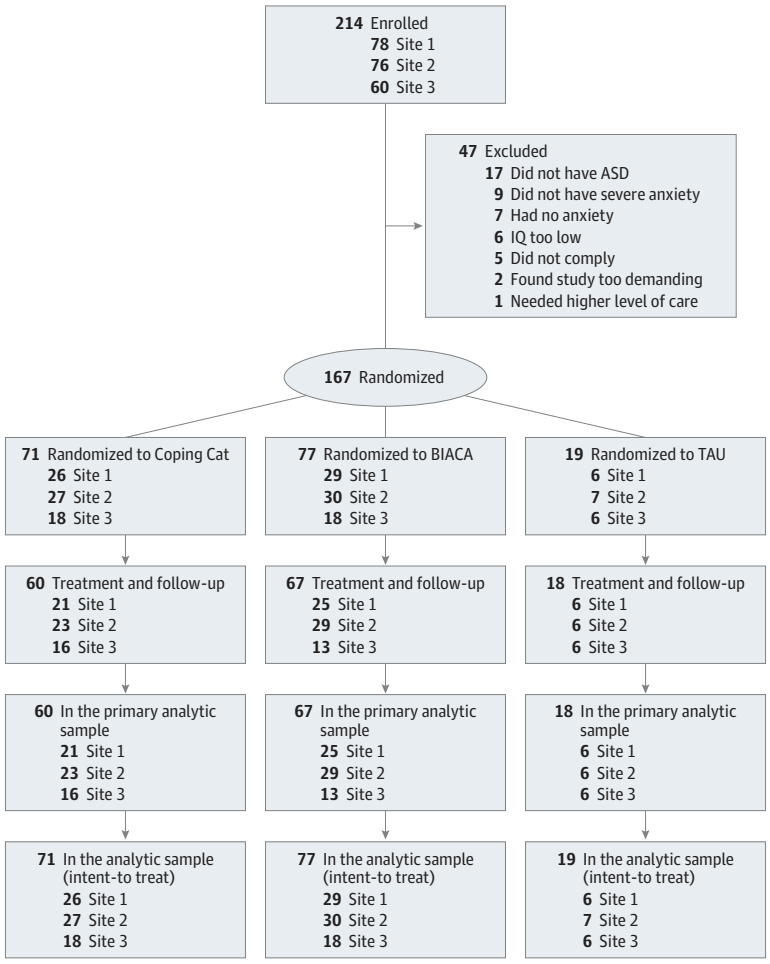
For secondary outcomes, the familywise error rate stemming from multiple comparisons was addressed, with the Holm-Bonferroni method applied separately to tests of deviation from the grand mean for the BIACA and Coping Cat groups (familywise α = .05). Follow-up contrasts, when performed, were protected with the Fisher least-significant-difference test approach. Because no significant findings were negated by these corrections, unadjusted P values were reported.

Statistical significance was defined as any P value less than .05 (2-tailed). Data analysis for this report occurred from December 2018 to February 2019. All analyses except GLMMs were calculated in SPSS version 24 (IBM).

Results

Table 1 presents demographic information for randomized families. Of those enrolled, 167 were randomized (64, 61, and

Figure 1. CONSORT Diagram



ASD indicates autism spectrum disorder; BIACA, Behavioral Interventions for Anxiety in Children with Autism; TAU, treatment as usual.

42 participants at the 3 study sites), 145 completed the study, and 22 discontinued participation (**Figure 1**). There was no significant difference in discontinuation across the BIACA, Coping Cat, and TAU conditions. A comparison of participants with complete and incomplete data are provided in eTable 1 in Supplement 2; those who discontinued early were more likely to be Latino or Latina (those who discontinued, 8 of 21 participants [38.0%]; those who completed, 22 of 144 participants [15.3%]; $P = .01$) and had higher baseline scores on the CAIS-School scale (mean [SD]: those who discontinued, 1.68 [0.75]; those who completed, 1.36 [0.59]; $P = .03$) and CAIS-Social scale (mean [SD]: those who discontinued, 1.30 [0.70]; those who completed, 0.89 [0.55]; $P = .003$).

Pretreatment sample characteristics (Table 1) yielded no condition differences or their interaction, with 1 exception: significant condition differences were found for child sex (female participants: BIACA group, 21 of 75 individuals [28%]; Coping Cat group, 13 of 72 individuals [18%]; TAU group, 0 of 19 individuals [0%]; $P = .03$), with a greater proportion of boys in TAU relative to other conditions. Sex was included as a covariate in subsequent analyses. There were several significant study-site differences on pretreatment characteristics (eTable 2 in Supplement 2). Participants at study site 1 were more likely to be Latino or Latina (site 1, 20 of 61 participants [33%]; site 2, 10 of 54 participants [16%]; site 3, 0 of 40 participants; $P < .001$), Asian/Pacific Islander (site 1, 9 of 61 participants [15%]; site 2, 1 of 64 participants [2%]; site 3, 0 of 40 participants; $P = .005$), or multiracial (site 1, 9 of 61 participants [15%]; site 2, 2 of 64 participants [3%]; site 3, 2 of 40 participants [5%]; $P = .04$), and less likely to be white (site 1, 40 of 61 participants [66%]; site 2, 54 of 64 participants [84%]; site 3, 34 of 40 participants [85%]; $P = .02$) or to have an annual household income below $40 000 (site 1, 6 of 59 participants [10%]; site 2, 18 of 63 participants [29%]; site 3, 9 of 40 participants [23%]; $P = .04$). Participants at study site 2 had higher pretreatment Childhood Autism Rating Scale scores than those at study site 1 (mean difference, 1.69 [95% CI, 0.05-3.33]; $P = .04$) and study site 3 (mean difference, 4.02 [95% CI, 2.20-5.84]; $P < .001$), while participants at study site 1 had higher pretreatment Childhood Autism Rating Scale scores than those at study site 3 (mean difference, 2.33 [95% CI, 0.55-4.11]; $P = .01$). Participants at study site 2 had higher pretreatment ADOS-2 algorithm scores than study site 1 (mean difference, 2.74 [95% CI, 1.40-4.07]; $P < .001$) and study site 3 (mean

difference [95% CI]: 3.60 [2.10-5.09]; $P < .001$), while participants at study site 1 and study site 3 did not differ. Study site was treated as a random effect in the GLMMs to incorporate these differences directly in the models.

At pretreatment, 65 of 165 children (27.5%) were using psychiatric medication (stimulants, 21 of 165 [12.7%]; selective serotonin reuptake inhibitors, 18 of 165 [10.9%]; α-agonists, 13 of 165 [7.9%]; atypical antipsychotics, 8 of 165 [4.8%]; anticonvulsants, 3 of 165 [1.8%]; monoamine reuptake inhibitors, 2 of 165 [1.2%]; and benzodiazepines, 1 of 165 [0.6%]). There were no significant condition or site differences in medication use.

Parents whose children were in the TAU group (17 parents) reported their service use at the posttreatment assessment. Overall, 12 of the 17 children received psychological or psychiatric care during the TAU period. One child began a new psychiatric medication, and 1 child changed a medication dosage. Eleven children received a psychological intervention (eg, psychotherapy), whereas 5 of 17 did not receive any services during TAU.

Therapists inquired about adverse events and completed a structured adverse event form after each CBT session. In terms of serious adverse events,[42] 1 was reported in the BIACA group (physical abuse by a teacher), and 1 was reported in the Coping Cat group (a child threatened to kill classmates but did not report an intention to take action). Both were reported to appropriate agencies. Neither was deemed to be study associated.

Primary and Secondary Outcomes

Table 2 provides descriptive statistics and 95% CIs for primary and secondary outcome measures. The model intercepts varied significantly among study sites for PARS scores (SD, 0.27; $P < .001$), CAIS-School scores (SD, 0.22; $P < .001$), and CAIS-Social scores (SD, 0.13; $P = .01$), indicating that mean posttreatment values, irrespective of treatment condition, differed among study sites for these outcomes.

However, random slopes for site were not significant, offering no evidence of differential treatment effects at specific sites; these were removed from final models. **Table 3** provides GLMM-based estimated differences from the grand mean at the posttreatment assessment for the BIACA and Coping Cat groups, and when those effects were significant, estimated group-mean differences using pairwise comparisons (ie, contrasts assessed with dummy coding). eTable 3 in Supplement 2 provides effect size estimates for all pairwise comparisons.

For the primary outcome measure (the independent evaluator-rated PARS score), there was a significant treatment effect for the BIACA group (difference from the grand mean, −0.352 [95% CI, −0.517 to −0.187]; $P < .001$) but not for the Coping Cat group (Table 3). Follow-up contrasts indicated that the BIACA group had better results than the Coping Cat group (*d*, 0.63 [95% CI, 0.27-0.99]; $P = .04$) and TAU (*d*, 1.69 [95% CI, 1.10-2.26]; $P < .001$; **Figure 2**; Table 3). Exploratory midtreatment analyses are presented in the eResults in Supplement 2.

Clinical Global Impression–Improvement

Because of separation problems in an initial nonlinear mixed model, the Fisher exact test was used for Clinical Global Impression-Improvement outcomes (response rates are in Table 2). Both the BIACA and Coping Cat groups had higher positive-response rates (61 of 66 participants [92.4%] and 47 of 58 participants [81.0%], respectively) than TAU (2 of 18 participants [11.1%]; $P < .001$ for each comparison), but the BIACA and Coping Cat groups did not significantly differ from each other. The absolute risk reduction estimates for no positive treatment response are 81% (95% CI, 58%-90%) for the BIACA group vs the TAU group and 70% (95% CI, 45%-81%) for the Coping Cat group vs the TAU group.

Child Behavior Checklist

For the 2 Child Behavior Checklist scales, there was a significant effect for the BIACA group (Anxious and Depressed scale, −0.134 [95% CI, −0.205 to −0.063]; $P < .001$; Internalizing scale, −0.074 [95% CI, −0.127 to −0.021]; $P = .007$) but not the Coping Cat group (Table 3). Follow-up contrasts indicated that the BIACA intervention outperformed the Coping Cat intervention on the Child Behavior Checklist Anxious and Depressed scale (*d*, 0.47 [95% CI, 0.10-0.83]; $P = .004$) and Internalizing scale (*d*, 0.50 [95% CI, 0.13-0.86]; $P = .01$). The BIACA intervention also outperformed TAU on these scales (Anxious and Depressed scale: *d*, 0.68 [95% CI, 0.13-1.22]; $P = .002$; Internalizing scale: *d*, 0.48 [95% CI, −0.07 to 1.01]; $P = .04$).

Social Responsiveness Scale–2

On the Social Responsiveness Scale-2 *DSM-5* Social Communication/Interaction scale, there was a significant effect of the BIACA intervention (Table 3). In follow-up contrasts, the BIACA intervention outperformed the Coping Cat intervention (*d*, 0.41 [95% CI, 0.04-0.77]; $P = .04$) and TAU (*d*, 0.61 [95% CI, 0.05-1.16]; $P = .008$). There was no effect of condition on the Social Responsiveness Scale-2 *DSM-5* Restricted/Repetitive Behavior scale scores.

CAIS

The outcome for the BIACA group differed significantly from the grand mean for the CAIS School and Social subscale scores (Table 3). For the CAIS School subscale, the BIACA intervention outperformed TAU (*d*, 0.75 [95% CI, 0.19-1.29]; $P = .003$), and the BIACA and Coping Cat interventions did not differ. On the CAIS Social subscale, the outcome for the BIACA group was significantly lower than that of the Coping Cat group (*d*, 0.28 [95% CI, −0.08 to 0.64]; $P = .04$) and TAU (*d*, 0.54 [95% CI, −0.01 to 1.07]; $P = .02$). There was no effect of condition on the CAIS Family scale scores.

Clinically Significant Improvement

Clinically significant improvement was examined in exploratory analyses by dichotomizing the posttreatment PARS Severity score according to whether children exhibited a greater than 35% reduction in values from baseline (ie, clinically significant anxiety reduction).[43] In the BIACA group, 35 of 66 children (53.0%) achieved this level of symptom relief, in comparison with 22 of 58 children (37.9%) in the Coping Cat group and 0 of 18 children in TAU ($P < .001$ by 3-condition likelihood ratio test). Both CBT treatments outperformed TAU. In post hoc analyses, children in the BIACA group who had

Table 2. Parameters for Primary and Secondary Outcome Measures for the 3 Treatment Groups Before and After Treatment

Scale	Behavioral Interventions for Anxiety in Children with Autism Group		Coping Cat Group		Treatment-as-Usual Group	
	Before Treatment	After Treatment	Before Treatment	After Treatment	Before Treatment	After Treatment
Pediatric Anxiety Rating Scale-Severity						
No. of participants	77	66	69	59	19	18
Mean (SD) [95% CI]	3.43 (0.48) [3.32-3.54]	2.13 (0.91) [1.91-2.36]	3.47 (0.47) [3.36-3.59]	2.43 (0.70) [2.25-2.62]	3.28 (0.39) [3.08-3.47]	2.93 (0.59) [2.63-3.22]
Child Behavior Checklist						
Anxious and Depressed scale						
No. of participants	76	63	69	55	17	17
Mean (SD) [95% CI]	0.83 (0.39) [0.74-0.92]	0.51 (0.29) [0.44-0.59]	0.88 (0.39) [0.79-0.97]	0.69 (0.34) [0.60-0.78]	0.73 (0.28) [0.59-0.87]	0.77 (0.27) [0.63-0.91]
Internalizing scale						
No. of participants	76	64	70	55	17	17
Mean (SD) [95% CI]	0.59 (0.28) [0.53-0.66]	0.37 (0.22) [0.32-0.43]	0.64 (0.26) [0.58-0.70]	0.50 (0.26) [0.43-0.57]	0.52 (0.19) [0.42-0.62]	0.50 (0.19) [0.40-0.60]
Social Responsiveness Scale-2						
Social Communication/ Interaction scale						
No. of participants	74	62	69	54	17	16
Mean (SD) [95% CI]	1.56 (0.33) [1.49-1.64]	1.32 (0.37) [1.23-1.42]	1.59 (0.38) [1.50-1.69]	1.46 (0.40) [1.35-1.57]	1.49 (0.28) [1.34-1.63]	1.53 (0.34) [1.35-1.71]
Restricted/ Repetitive Behavior scale						
No. of participants	74	62	69	54	16	16
Mean (SD) [95% CI]	1.39 (0.44) [1.29-1.49]	1.15 (0.45) [1.04-1.27]	1.51 (0.43) [1.41-1.62]	1.30 (0.46) [1.18-1.43]	1.25 (0.47) [1.00-1.50]	1.16 (0.38) [0.96-1.36]
Child Anxiety Impact Scale						
School						
No. of participants	76	63	69	54	18	17
Mean (SD) [95% CI]	1.38 (0.61) [1.25-1.52]	0.77 (0.57) [0.63-0.92]	1.48 (0.60) [1.34-1.62]	0.88 (0.54) [0.74-1.03]	1.19 (0.70) [0.84-1.54]	1.24 (0.51) [0.97-1.50]
Social						
No. of participants	76	64	70	55	17	17
Mean (SD) [95% CI]	0.97 (0.56) [0.85-1.10]	0.49 (0.42) [0.38-0.59]	0.96 (0.62) [0.82-1.11]	0.65 (0.54) [0.51-0.80]	0.70 (0.54) [0.43-0.98]	0.80 (0.50) [0.54-1.05]
Family						
No. of participants	75	64	70	55	18	17
Mean (SD) [95% CI]	1.16 (0.63) [1.01-1.31]	0.65 (0.49) [0.53-0.77]	1.12 (0.62) [0.97-1.27]	0.73 (0.51) [0.60-0.87]	0.98 (0.44) [0.76-1.20]	0.88 (0.60) [0.57-1.19]
Clinical Global Impressions-Improvement						
Positive treatment response, No./total No. (%)	NA	61/66 (92.4)	NA	47/58 (81.0)	NA	2/18 (11.1)

Abbreviation: NA, not applicable.

achieved clinically significant anxiety reduction by this metric exhibited a pattern of consistent and moderate to large differences on secondary outcome measures in comparison with children in the BIACA group who had not done so; this pattern was less distinct in the Coping Cat group (eTable 4 in Supplement 2).

Sensitivity Analyses

In the intent-to-treat analyses conducted as described, all significant contrasts from the GLMMs remained, with 1 exception. The contrast between the participants in the BIACA and TAU groups on the Child Behavior Checklist–Internalizing scale was not significant.

Discussion

The present findings indicate that both versions of a psychological therapy, CBT, are beneficial for children with ASD and maladaptive anxiety. Both CBT conditions had positive effects, but an adapted CBT program (BIACA) outperformed standard-of-practice CBT (Coping Cat) and TAU on the primary outcome measure (independent evaluator–rated PARS scores) and several parent-reports of associated emotion dysregulation symptoms, social-communication symptoms, and adaptive functioning. Both CBT conditions achieved higher rates of positive treatment response on the Clinical Global Impression-

Table 3. Summary Table for General Linear Mixed Models Comparing Treatment Conditions at Posttreatment, Controlling for Baseline Score and Sex[a]

Measure	Expected Differences From Grand Mean After Treatment[b]				Contrasts: Expected Group Mean Differences After Treatment[c]			
	BIACA vs Grand Mean		Coping Cat vs Grand Mean		BIACA vs Coping Cat		BIACA vs Treatment as Usual	
	Mean Difference (95% CI)	*P* Value	Mean Difference (95% CI)	*P* Value	Mean Difference (95% CI)	*P* Value	Mean Difference (95% CI)	*P* Value
Pediatric Anxiety Rating Scale								
Severity	−0.352 (−0.517 to −0.187)	<.001	−0.103 (−0.266 to 0.060)	.22	−0.249 (−0.488 to −0.010)	.04	−0.806 (−1.165 to −0.447)	<.001
Child Behavior Checklist								
Anxious and Depressed scale	−0.134 (−0.205 to −0.063)	<.001	0.018 (−0.055 to 0.091)	.63	−0.151 (−0.251 to −0.051)	.004	−0.249 (−0.406 to −0.092)	.002
Internalizing scale	−0.074 (−0.127 to −0.021)	.007	0.023 (−0.030 to 0.076)	.41	−0.097 (−0.172 to −0.023)	.01	−0.126 (−0.243 to −0.010)	.04
Social Responsiveness Scale-2								
Social Communication/ Interaction scale	−0.117 (−0.195 to −0.039)	.004	−0.002 (−0.076 to 0.080)	.96	−0.115 (−0.223 to −0.007)	.04	−0.235 (−0.406 to −0.065)	.008
Restricted/ Repetitive Behavior scale	−0.049 (−0.147 to 0.049)	.34	0.029 (−0.071 to 0.129)	.57	NA	NA	NA	NA
Child Anxiety Impact Scale								
School	−0.163 (−0.288 to −0.038)	.01	−0.091 (−0.216 to 0.034)	.16	−0.070 (−0.248 to 0.108)	.44	−0.416 (−0.688 to −0.144)	<.001
Social	−0.149 (−0.255 to −0.043)	.006	0.011 (−0.117 to 0.095)	.83	−0.160 (−0.307 to −0.013)	.04	−0.284 (−0.515 to −0.053)	.02
Family	−0.095 (−0.205 to 0.015)	.09	−0.018 (−0.128 to 0.092)	.74	NA	NA	NA	NA

Abbreviation: BIACA, Behavioral Interventions for Anxiety in Children with Autism.

[a] Study site was treated as a random effect in all models. The posttreatment numbers of participants provided in Table 2 reflect sample sizes for each analysis.

[b] Deviation effect coding was used in general linear mixed models to test treatment effects, with the BIACA and Coping Cat arms compared with the grand mean through the following effect coding for BIACA, Coping Cat, and treatment as usual, respectively: (0, 1, −1) and (1, 0, −1).

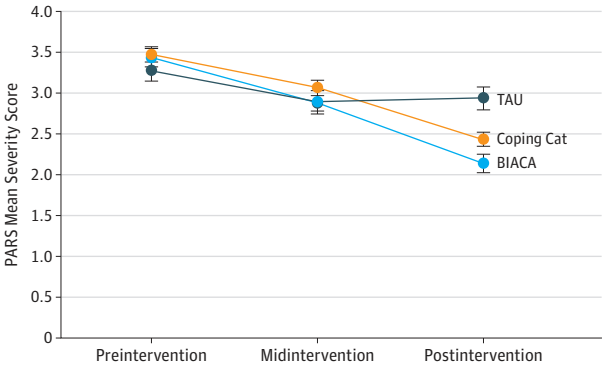
[c] Significant treatment effects for the BIACA or Coping Cat interventions were followed with contrasts in comparable general linear mixed models using dummy coding to make specific comparisons between conditions (eg, BIACA vs Coping Cat and vs treatment as usual). Estimated group differences for posttreatment mean scores from the models represent the following minueds and subtrahends: BIACA minus the grand mean, Coping Cat minus the grand mean, BIACA minus Coping Cat, BIACA minus treatment as usual. A column for Coping Cat minus treatment as usual contrasts was omitted because none of the primary general linear mixed models using deviation effect coding had significant treatment outcomes for Coping Cat.

Improvement (each greater than 80%) than TAU (11%). Accordingly, CBT was found to be beneficial for youth with ASD and anxiety, with an adapted CBT approach showing additional advantages.

Consistent with evidentiary standards for assessing treatment efficacy,[19] this study compared 2 treatments and an active comparator (TAU), had an adequately powered sample, included experts in the treatments being investigated, assessed treatment integrity, and used independent evaluators, lending weight to the findings in comparison with preliminary trials.[14] The comparison of adapted CBT and standard-of-practice CBT in particular provides a more stringent test of efficacy than previous trials.[19] The relative benefit of adapted CBT relative to standard-of-practice CBT was moderate in terms of effect size for the primary outcome measure, with additional advantages in terms of effects on social-communication symptoms and adaptive outcomes. That groups did not differ on PARS scores at midtreatment suggests the need for continued intervention to access full benefits.

The capacity of BIACA to address social-communication symptoms is important, given the synergy between social-communication challenges and anxiety in children with and without ASD.[5-8,14,21] Improvements in social-communication functioning did not parallel anxiety reduction to the same degree in the Coping Cat intervention. The BIACA intervention supports social-communication skills through targeted use of evidence-based practices addressing peer engagement, friendship, and perspective taking. Improving social functioning may be a pathway to anxiety reduction as well as a goal unto itself; however, anxiety reduction alone may not result in comparable improvements in social functioning in children with ASD.

Figure 2. Pediatric Anxiety Rating Scale Scores Before, During and After Treatment in the Treatment-as-Usual (TAU), Coping Cat, and Behavioral Interventions for Anxiety in Children with Autism (BIACA) Groups



PARS indicates Pediatric Anxiety Rating Scale.

Given the positive effects of the adapted CBT program, what features might contribute to its benefits? The BIACA intervention is modular, with components apportioned based on need; some research has identified advantages of modular programs.[44] Second, the BIACA program is tailored to children with ASD (eg, it addresses social communication, integrates parents more into treatment sessions, incorporates children's special interests). Additionally, BIACA treatment sessions were 50% longer than Coping Cat sessions (90 minutes compared with 60 minutes). The current findings support the benefit of the additional time spent in treatment. For youth with ASD, the added time for parent involvement and an expanded scope of treatment targets may contribute the added outcomes.

Limitations

Limitations merit consideration. The difference in the duration of treatment sessions and the magnitude of parental inclusion may be seen as a confound, particularly given the use of parent-reported outcome measures; however, these differences are explicit features of the CBT conditions, and some outcomes were specific, as opposed to universally more favorable in the BIACA arm. To facilitate generalizations about the treatments, both CBT conditions were implemented according to their protocols. Furthermore, the specificity of treatment effects to ASD populations was not assessed, although these modifications may also benefit children with milder social-communication difficulties.[21] The sample was not as diverse as we would have preferred and was mostly male (consistent with typical ASD sex ratios), including having no female participants in the TAU arm, leading to a sex imbalance among conditions (which were controlled for in analyses). The TAU condition is also heterogeneous; however, TAU is a relatively stringent comparator.[40]

Conclusions

Cognitive-behavioral therapy appears to be a frontline treatment for verbal children with ASD and maladaptive and interfering anxiety. Positive response was achieved after manual-based CBT provided by therapists with modest training and weekly supervision. Therapists involved in clinical research with expert supervision may be well prepared to implement CBT for children with ASD; extending these findings to community clinicians without specific ASD expertise is a necessary next step. To this end, a training and clinician guidance app has been developed for community clinicians and is available free of charge at https://meya.ucla.edu/. Although supervision opportunities and expert training are not yet widely accessible, the benefits of CBT appear to justify efforts to disseminate relevant protocols in clinical settings where children with ASD receive services.

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Acquisition, analysis, or interpretation of data: J. Wood, K. Wood, Kerns, Seltzer, Small, Lewin, Storch.
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