Treatment of Anxiety Disorders in Youths: Filling the Cup Further

Neal D. Ryan, M.D.

Current treatments for anxiety disorders with demonstrated efficacy in youths include selective serotonin reuptake inhibitors (SSRIs) and cognitive-behavioral therapy (CBT). When used in the treatment of child and adolescent anxiety disorders, they have response rates of 50%−70% (1, 2). Combined treatment with an SSRI and CBT offers response rates as high as 80% (1). Remission rates are lower, but the rate exceeds 50% over time for SSRI or CBT and is approximately 70% for the combination treatment (3). These response and remission rates are soundly above the "cup half full" level. Yet they also leave many youths with partially responsive or unresponsive anxiety disorders despite state-of-the-art treatment. Therefore, an augmentation treatment boosting the overall response and remission rates, especially one that works through a different mechanism, would be of great clinical and scientific interest.

The article by White et al. in this issue (4) looks at augmentation of standard CBT for anxiety disorders in youths with either attention bias modification treatment (ABMT) or a placebo ABMT treatment, examining the relationship between amygdala-insula connectivity findings on the dot-probe imaging task and treatment outcome.

Youths with anxiety disorders show implicit or involuntary bias toward threatening pictures (typically pictures of angry faces) compared with healthy youths as assessed by the dot-probe task. In that task, two images of faces are presented briefly while the subject stares at a fixation point midway between them. As used in this study, these are two images of the same actor, one image showing a neutral expression and the other an angry expression. After the images disappear, a visual stimulus is presented at the location where one of the two images was shown, and the subject makes a response indicating the directionality of the stimulus (either "<" or ">"). Attention bias to the angry facial image is shown by more rapid response when the stimulus is in the location where the angry-face picture was presented.

ABMT adapts the dot-probe task to implicitly teach the subject to pay more attention to the neutral stimuli and less to the threatening stimuli—to correct involuntary biases by making the location of the task-relevant target always the neutral face, never the angry face. CBT targets voluntary components of attention as well as having an exposure component.

ABMT has been studied both as a stand-alone treatment and in combination with other treatments. In a 2015 meta-analysis, ABMT as a stand-alone treatment for anxiety disorders showed significant anxiety symptom reduction by clinician evaluation but not by patient self-report (5). Two studies, both very small, have examined ABMT augmentation strategies. One added ABMT to usual treatment in a residential treatment program, compared with usual treatment plus attention control (N=21 in each arm) and found greater improvement in anxiety symptoms in the ABMT augmentation group (6). The other study, which compared ABMT plus CBT (N=18) and placebo ABMT plus CBT (N=25) in adolescents seeking treatment in a child anxiety clinic, found no difference between groups in number or severity of symptoms as assessed by Anxiety Disorders Interview Schedule but greater improvement in anxiety scores on the Screen for Child Anxiety Related Disorders in the ABMT plus CBT group (7).

This study adds to the available data suggesting that the addition of ABMT to CBT increases the overall response rate of anxiety disorders in youths.

The White et al. study included medication-free youths with generalized anxiety disorder, social anxiety, and/or separation anxiety without current major depressive disorder, obsessive-compulsive disorder, or posttraumatic stress disorder. Forty-three participants were randomly assigned to receive CBT plus ABMT and 42 to receive CBT plus placebo ABMT. The treatment consisted of 12 sessions of CBT using the CBT protocol from the Child/Adolescent Anxiety Multimodal Study (1). ABMT or placebo ABMT was delivered in two 5-minute sessions within CBT sessions 4 through 12, one before the CBT and one immediately after. Placebo ABMT was constructed by locating the probe on the angry face side and the neutral face side 50% of the time each instead of locating the probe on the neutral face side 100% of the time for ABMT.

Both treatment groups improved over the course of treatment. The CBT plus ABMT group had significantly lower posttreatment Pediatric Anxiety Rating Scale ratings compared with the CBT plus placebo ABMT group, a difference of medium effect size. Categorical response analysis based on the improvement item of the Clinical Global Impressions scale showed no between-group differences.

Paralleling previous studies, patients in the White et al. study showed greater positive right amygdala-insula connectivity on

trials when the probe was in the location of the angry face ("congruent trials"), and healthy control subjects showed greater positive amygdala-insula connectivity when the probe was in the location of the neutral face ("incongruent trials"). There were other findings related to connectivity patterns and response to treatment, particularly in the group receiving placebo ABMT. As noted by the authors, the sample size for these comparisons was modest (usable pretreatment functional MRI [fMRI] data were available for 24 patients in the ABMT group and 30 in the placebo ABMT group).

The important take-home messages of this study include the following:

- ABMT is a treatment developed based on understanding of neural circuitry underlying anxiety disorders; it may work through distinctly different pathways than other available treatments. It requires surprisingly little time to deliver; in this study the ABMT augmentation consisted of 18 sessions, each lasting 5 minutes.
- This study adds to the available data suggesting that the addition of ABMT to CBT increases the overall response rate of anxiety disorders in youths.
- The imaging data in this study provide additional support for the hypothesis that ABMT works through different mechanisms than CBT and strongly supports similar fMRI measures being incorporated in larger future trials of ABMT augmentation.

There are many ways to improve overall treatment response in specific psychiatric disorders. The aggregation of many small improvements can together add up to substantial gains. In addition, new treatments working through new pathways offer the potential of making a substantial improvement in a single step. ABMT may ultimately prove to offer this sort of large step in our treatment optimization.

AUTHOR AND ARTICLE INFORMATION

From the Western Psychiatric Institute and Clinic, University of Pittsburgh Medical Center, Pittsburgh.

Address correspondence to Dr. Ryan (ryannd@upmc.edu).

The author reports no financial relationships with commercial interests.

Accepted May 2017.

Am J Psychiatry 2017; 174:723–724; doi: 10.1176/appi.ajp.2017.17050544

REFERENCES

1. Walkup JT, Albano AM, Piacentini J, et al: Cognitive behavioral therapy, sertraline, or a combination in childhood anxiety. N Engl J Med 2008; 359:2753–2766
2. Silk JS, Tan PZ, Ladouceur CD, et al: A randomized clinical trial comparing individual cognitive behavioral therapy and child-centered therapy for child anxiety disorders. J Clin Child Adolesc Psychol (Epub ahead of print, March 16, 2016)
3. Piacentini J, Bennett S, Compton SN, et al: 24- and 36-week outcomes for the Child/Adolescent Anxiety Multimodal Study (CAMS). J Am Acad Child Adolesc Psychiatry 2014; 53:297–310
4. White LK, Sequeira S, Britton JC, et al: Complementary features of attention bias modification therapy and cognitive-behavioral therapy in pediatric anxiety disorders. Am J Psychiatry 2017; 174: 775–784
5. Linetzky M, Pergamin-Hight L, Pine DS, et al: Quantitative evaluation of the clinical efficacy of attention bias modification treatment for anxiety disorders. Depress Anxiety 2015; 32:383–391
6. Riemann BC, Kuckertz JM, Rozenman M, et al: Augmentation of youth cognitive behavioral and pharmacological interventions with attention modification: a preliminary investigation. Depress Anxiety 2013; 30:822–828
7. Shechner T, Rimon-Chakir A, Britton JC, et al: Attention bias modification treatment augmenting effects on cognitive behavioral therapy in children with anxiety: randomized controlled trial. J Am Acad Child Adolesc Psychiatry 2014; 53:61–71