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Review

Pooled patient-level meta-analysis of children and adults completing a computer-based anxiety intervention targeting attentional bias

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HIGHLIGHTS

- Transdiagnostic remission was 2.5 times higher for active modification vs. control.
- Anxiety decreased only when training sessions were completed in the laboratory.
- Social anxiety decreased significantly only in participants <37 years old.
- Reductions in anxiety were mediated by reductions in the intervention mechanism, attention bias.

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ABSTRACT

Computer-based approaches, such as Attention Bias Modification (ABM), could help improve access to care for anxiety. Study-level meta-analyses of ABM have produced conflicting findings and leave critical questions unresolved regarding ABM's mechanisms of action and clinical potential. We pooled patient-level datasets from randomized controlled trials of children and adults with high-anxiety. Attentional bias (AB) towards threat, the target mechanism of ABM, was tested as an outcome and a mechanistic mediator and moderator of anxiety reduction. Diagnostic remission and Liebowitz Social Anxiety Scale (LSAS) were clinical outcomes available in enough studies to enable pooling. Per-patient data were obtained on at least one outcome from 13/16 eligible studies [86% of eligible participants; n = 778]. Significant main effects of ABM on diagnostic remission (ABM—22.6%, control—10.8%; OR = 2.57; $p = 0.006$) and AB (β^* (95%CI) = −0.63 (−0.83, −0.42); $p < 0.00005$) were observed. There was no main effect of ABM on LSAS. However, moderator analyses suggested ABM was effective for patients who were younger (≤37 y), trained in the lab, and/or assessed by clinicians. Under the same conditions where ABM was effective, mechanistic links between AB and anxiety reduction were supported. Under these specific circumstances, ABM reduces anxiety and acts through its target mechanism, supporting ABM's theoretical basis while simultaneously suggesting clinical indications and refinements to improve its currently limited clinical potential.

Contents

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1. Introduction

Anxiety disorders are the most prevalent class of mental health disorders (Kessler, Chiu, Demler, Merikangas, & Walters, 2005), affecting approximately 812 million individuals annually worldwide (Baxter, Scott, Vos, & Whiteford, 2013). Clinical and subclinical forms of anxiety are associated with significant medical morbidity, disability, and public health burden (Kessler, 2007), with an estimated direct societal cost of over $42 billion per year in the U.S. (Greenberg et al., 1999). Efficacious treatments for anxiety, including cognitive-behavioral therapies and pharmacotherapy, have been available for decades, yet disorder prevalence rates remain notably consistent, with only 12.7% of patients receiving minimally adequate treatment (Wang et al., 2005). This observation has led to a call for interventions that take advantage of technology to increase patient access, reduce cost, and minimize aversive consequences, through the use of automated, computer-based procedures (Mohr, Burns, Schueller, Clarke, & Klinkman, 2013).

Current first-line treatments for clinical anxiety exhibit a 50–70% response plateau (Ballenger, 2004; Barlow, Gorman, Shear, & Woods, 2000; Hofmann & Smits, 2008; McEvoy, 2007), with high rates of relapse, low rates of remission, and little evidence to suggest which patients may benefit from which treatment options. These patterns underscore the need to continue refining existing treatments and developing novel interventions. Barriers to progress towards a more efficient and effective approach to anxiety treatment may include inadequate focus on theory-driven, mechanistic predictors of treatment outcome; the use of heterogeneous treatment protocols that require expert administration and have multiple likely mechanisms; and the current diagnostic nosology of psychiatry, which may obscure critical, transdiagnostic dimensions of biobehavioral functioning (Insel et al., 2010). Many recent clinical research efforts have therefore increasingly focused on mechanistic treatments, which are designed to target a well-defined, unitary mechanism, often with transdiagnostic relevance. Mechanistic intervention studies carry the potential to inform both the theory of conditions like anxiety—providing an experimental test of causality—and the clinical practice of how to efficiently deliver the "right" treatment to the "right" patient.

One such mechanistic intervention, Attention Bias Modification (ABM) (MacLeod & Clarke, 2015), is designed to directly target a well-replicated, posited mechanism of anxiety: selective attention to threat. Anxious individuals, across a wide range of clinical and subclinical definitions, exhibit attentional preferences towards threatening information (henceforth, 'attentional bias'; AB) (Bar-Haim, Lamy, Pergamin, Bakermans-Kranenburg, & van IJzendoorn, 2007). ABM seeks to modify this AB through repeated attention retraining exercises. If AB plays a causal role in promoting anxiety (e.g., by fostering exaggerated perceptions of danger), reduction of AB should lead to reduction of symptoms. This approach represents a departure from gold-standard behavioral treatments for anxiety (e.g., cognitive-behavioral therapy), as it relies solely on implicit training of a cognitive pattern as opposed to effortful changes to thoughts and behaviors, and might therefore be beneficial and/or appealing to a distinct subset of patients. After an initial demonstration (MacLeod, Rutherford, Campbell, Ebsworthy, & Holker, 2002) in healthy individuals that AB could be experimentally manipulated using automated procedures, producing downstream effects on mood reactivity, intervention studies in clinical populations followed. Initial findings in small samples suggested the potential to ameliorate clinical symptoms, and even reverse clinical diagnoses (Amir, Beard, Burns, & Bomyea, 2009b; Amir et al., 2009a). However, larger subsequent studies, many using home/Internet-based administration, did not consistently confirm these findings (Clarke, Notebaert, & Macleod, 2014).

Considerable controversy remains regarding whether further research and clinical resources should be devoted to ABM. Central questions relevant to such a 'go/no-go' decision have not yet been resolved through standard study-level meta-analytic approaches. In spite of at least seven published meta-analyses examining the effects of ABM on measures of anxiety (Beard, Sawyer, & Hofmann, 2012; Cristea, Kok, & Cuijpers, 2015; Hakamata et al., 2010; Hallion & Ruscio, 2011; Heeren, Mogoase, Philippot, & McNally, 2015; Linetzky, Pergamin-Hight, Pine, & Bar-Haim, 2015; Mogoaşe, David, & Koster, 2014), meta-analytic conclusions have differed dramatically, ranging from no reliable effect on anxiety (Cristea et al., 2015), to effect sizes rivaling those of first-line anxiety treatments (Hakamata et al., 2010), to modest effects under constrained conditions (e.g., when training is delivered in the laboratory rather than at home; when anxiety is assessed by clinician ratings rather than self-report) (Heeren et al., 2015b; Linetzky et al., 2015). Ongoing debate is particularly focused around two key issues with clinical, pragmatic, and theoretical relevance: 1) whether the effects of ABM are clinically meaningful, for at least a subset of anxious patients—a question with relevance to clinical decision-making, particularly if subsets of anxious patients likely to benefit can be defined according to concrete, readily obtainable indices; and 2) whether symptom improvements are contingent upon successful change in the target mechanism (AB). This latter question is fundamental to the theoretical basis and future of ABM research; if supported, it would suggest that the mechanistic target of ABM (AB reduction) is valid, producing concomitant symptom relief when it is successfully ameliorated, while the ability to reliably manipulate the target is what requires further refinement (MacLeod & Clarke, 2015). While a subset of individual studies have reported evidence of such mediational patterns (Amir et al., 2009a; Amir et al., 2009b; Kuckertz et al., 2014), many either do not assess this question or report null effects (and even among studies reporting mediation, findings have been inconsistent across anxiety scales). This is unsurprising given the substantial power constraints for testing mediation in small samples. Notably, both mechanistic and individualized prognostic questions are quite difficult to address using a standard meta-analytic