Testing Theory or Changing the World?
Balancing the Competing Goals of Psychotherapy Research
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Historically, psychotherapy research has been defined by three core questions. Can psychotherapy work (efficacy)? Does psychotherapy work in practice (effectiveness)? And, how does psychotherapy work (mechanism)? Doss and Atkins (2006) bring together two of these questions and offer guidelines for testing treatment mechanism in effectiveness settings and other contexts in which random assignment may be difficult. This commentary reflects on the underlying issue of balancing the demands of theory testing and practice relevance in psychotherapy research. Examples from the adolescent depression literature illustrate (a) how a shifting base of knowledge may restructure questions of efficacy, effectiveness, and mechanism, and (b) the value of taking a psychopathology-specific view of the challenges and opportunities involved in the design of mechanism studies.

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As an applied science, clinical psychology is the servant of two masters. Arguably, the primary goal of clinical research is to serve the public interest—to produce practice-relevant knowledge designed to improve the effectiveness of interventions and reduce the public health burden of mental disorder. However, on at least a part-time basis, clinical scientists are devoted to developing and testing psychological theories. These public health and theory-testing goals of clinical research are frequently in dynamic tension, as aptly illustrated in the article by Doss and Atkins (2006) on the challenges of investigating treatment mediation in the current clinical research climate. The authors critique commonly accepted methods for demonstrating mediation (e.g., Baron & Kenny, 1986; Kraemer, Wilson, Fairburn, & Agras, 2002) and suggest a variety of quasi-experimental designs for inferring likely mediation, when ethical and practical constraints make the use of traditional designs and analytic approaches difficult to implement. In this commentary, I provide a brief critique of the authors’ arguments and suggested solutions; however, I focus the bulk of my remarks on what I view as the central question underlying their article: How can the demands of public health relevance and theory testing be reconciled in modern psychotherapy research?

A SERVANT OF TWO MASTERS

In no area of psychological investigation is the tension between theory and application more evident than in therapy research. Although the gap between research laboratory and clinical office is wide and well documented, findings from randomized controlled trials (RCTs) of psychotherapy have increasingly found their way into the real world and served as the basis for professional treatment guidelines, public policy, and the availability of and reimbursement for mental health services (for discussion, see Weisz, Weersing, & Henggeler, 2005). In addition to informing these public health decisions, RCTs offer investigators a unique opportunity to conduct theoretically meaningful psychopathology experiments in human samples. For this purpose, the independent variable of therapy is conceived not simply as a potential public health intervention, but rather as a manipulation of the processes maintaining psychological dysfunction.

Of course, it is the rare modern study that seeks to achieve only one of these two goals. Psychotherapy studies are “hard science” at least in terms of their difficulty—they are complex to execute, expensive to conduct, and require years to complete. Furthermore, any experimentation on humans raises ethical questions, concerns that are only magnified in research with patient samples. As a result of these high stakes, a therapy trial often tries to answer as many questions as possible in its single shot at success and to achieve both theory testing and public health–relevant aims.
This pragmatic strategy seems to lie at the heart of the Doss and Atkins (2006) critique of mediation methods. Indeed, the rationale for and recommendations of the article are framed primarily in terms of working around practice-relevant constraints on theory testing—for example, coping with organizational factors that may limit the ability of investigators to randomize patients to certain theoretically desirable control conditions. Notably, the critique also adopts an explicitly measurement-focused approach toward investigating mechanisms of psychotherapy. In the article, mediator and patient outcomes are directly assessed over the course of treatment, and, by examining the logical (e.g., temporal sequencing) and statistical associations between the measures of mediator and outcome, conclusions about the processes of therapeutic change may be inferred. The Doss and Atkins review is refreshing in its rejection of a “one design fits all” approach to psychotherapy mechanism research and explicit description of how mediation may be obscured in certain designs and circumstances. This said, their pragmatic compromise between theory testing and practice relevance may be a better fit to some clusters of psychopathology and domains of treatment research than others. As an example, consider briefly the extraordinary reversals in the adolescent depression treatment literature that have occurred over the last two years.

A CAUTIONARY TALE: TREATMENT OF DEPRESSION IN ADOLESCENTS

Until recently, cognitive-behavioral therapy (CBT) was generally considered to be a highly efficacious intervention for depressed adolescents (e.g., Compton et al., 2004). Focused meta-analyses reported effect sizes for CBT that were among the largest in the youth psychotherapy literature (e.g., Reinecke, Ryan, & DuBois, 1998), and support for CBT within the clinical psychology research community was strengthened by growing concerns about the safety of selective serotonin reuptake inhibitors (SSRI) in youth (see, for example, National Institute for Health and Clinical Excellence, 2005). Within the last two years, however, a series of new findings have complicated this sunny picture of CBT. The most well-known results come from the large Treatment for Adolescents with Depression Study (TADS, 2004). In TADS, CBT failed to outperform a pill placebo, while active medication protocols (fluoxetine alone and fluoxetine + CBT) produced strong effects. Secondary analyses of the TADS data suggested value in adding CBT to medication, but, overall, these results appeared to stand in sharp contrast to the previous 20 years of research on the positive effects of CBT in treating depressed children and adolescents. Even more recently, a comprehensive review of the youth depression literature has suggested that previous meta-analyses may have overestimated the size of CBT effects by 300%. Although CBT did demonstrate a significant effect compared to control conditions in this review, what were once the largest effects in the youth psychotherapy literature are now reported to be among the smallest (Weisz, McCarty, & Valeri, 2006). Explanations abound for CBT’s reversal of fortune, with hypotheses focusing mainly on (a) possible increases in the severity of depression treatment samples since the conduct of the original CBT studies (cf., Bridge & Brent, 2004; TADS, 2004) or (b) differences between CBT treatment manuals in content, active ingredients, and efficacy (Hollon, Garber, & Shelton, 2005; Weersing & Brent, in press).

This cautionary tale serves to illustrate several points related to the appropriate balance between theory testing and practice relevance in clinical research. First, in many areas of psychotherapy research, we may be well advised to cling to our theoretically relevant control conditions, rather than moving quickly to embrace practice-relevant treatment-treatment comparisons. When therapy is viewed as a theoretical manipulation, the control condition of an RCT should be similarly defined by the presence or absence of theory-relevant components. Control groups in this formulation are designed both to ward off threats to internal validity (e.g., maturation, history, and impact of repeated assessments) and to enhance the construct validity of the experimental comparison (e.g., by ruling out competing theoretical explanations for observed effects).

As one can easily imagine, control conditions designed to achieve these methodological aims may not always have the greatest public health relevance. For example, based on the known efficacy of CBT, TADS was designed as a blended efficacy-effectiveness hybrid (i.e., to serve theory testing and public health goals). In this spirit, the design was not fully crossed, and the study omitted a theoretically meaningful, but public health irrelevant, control group—the combination of CBT and pill placebo. Given the results of TADS, this control group would be quite useful in ruling out possible explanations for the
poor response of CBT. In the hybrid design, youth in CBT were the only participants in the study who could be sure that they were not receiving antidepressant medication, and this inconsistent blinding of participants to treatment condition may have produced differential expectations for success, investment in treatment, and contributed to poor outcome. In combination with other unique characteristics of the TADS sample and treatment program, this design choice is a significant barrier to understanding the theoretical implications of the findings. However, given what was known about the effects of CBT when TADS was being designed, exclusion of a CBT + placebo group can be viewed as reasonable from a public health perspective. The control condition of a public health–focused RCT is designed to produce clear and useful practice-relevant conclusions. In this case, comparison of a new or refined intervention, such as fluoxetine + CBT, to another therapy or therapies with established efficacy, such as CBT alone or medication alone, may serve as sufficient control and a public health gold standard. In contrast, CBT + placebo is not a viable treatment about which practitioners need evidence-based decision rules. Of course, the difficulty in balancing theory testing against practice relevance arises when we do not know what we do not know about the effects of psychotherapy.

A second implication, drawn from the broader adolescent depression literature, is that our therapy research designs may need to be more closely informed by theories of psychopathology than by broad theories of intervention. For example, depression is fundamentally an episodic disorder, and depression clinical trials must take into consideration the high rates of natural remission that occur without formal treatment. Indeed, in the SSRI literature on the treatment of adolescent depression, the depression recovery rate in the pill placebo control group is the best predictor of whether an investigation will find significant effects (Bridge et al., 2006). In other words, the greatest contributor to the effect size of an SSRI trial may not be the actual magnitude of the treatment effect, but rather the poorly understood processes of recovery occurring in the control condition. This characteristic of depression sets it apart from other potential pathology targets and presents both specific challenges and unique opportunities for the investigation of therapy mechanism. To my knowledge, there has yet to be a study that unpacks the “change processes” (Doss, 2004) of minimal contact placebo conditions in depression or assesses the extent to which change in possible mediators (e.g., response to stressful life events, cognitive processes, and behavioral avoidance) is differentially associated with outcome in therapy versus placebo.

As a final, related point, this depression treatment example also is useful in demonstrating the value of stepping outside of psychological interventions and psychological mediators when trying to design investigations to understand mechanisms of therapeutic action. Several of the problems delineated by Doss and Atkins (2006) in testing mediation in treatment–treatment comparisons are substantially reduced when one of the treatments in question is medication (or pill placebo) and the other psychotherapy. While medication and therapy may be found to eventually affect the same biological substrates, that final common pathway is the far end of a chain of change processes that would likely significantly differ between these two interventions and provide a host of opportunities to investigate mediated effects, while still complying with ethical and organizational pressures to provide treatment to all participants. Of course, not every target of psychotherapy is a condition for which medication is a suitable intervention.

**BRINGING EVERY TOOL TO BEAR**

This commentary may be seen by some as a suggestion to step away from the complications associated with practice-relevant settings when investigating therapy mechanisms. This has not been my intent. To paraphrase Lewin (1943), my aim has been to argue that “there is nothing as practical as [the test of] a good theory” and that our best tests of theory involve the most rigorous methods that can be brought to bear in any given situation. In addition to the quasi-experimental strategies clearly described by Doss and Atkins (2006), there is value in continuing to carefully craft experimental control conditions to test rival hypotheses of therapeutic action involved in the treatment of specific domains of psychopathology (e.g., adult depression; Dimidjian et al., 2006). As noted by the authors, this type of design is subject to the awkward subtraction that characterizes all null-hypothesis testing strategies. A finding of significant difference between conditions only highlights what you have removed from (or added to) therapy, not the
contribution of what remains constant between conditions. To experimentally investigate the effects of common elements across treatment packages (i.e., the role of behavioral activation in both CBT and interpersonal therapy) may require the creation of “theoretical chimera” — control conditions with specific theoretical relevance, but that may have little practical purpose or likelihood of ever being used as a public health intervention. Furthermore, findings of experimental group differences in global processes and outcomes still need to be paired with consideration of the logical relationships that should be evident in treatment mediation: (a) association between measures of process and outcome (Weersing & Weisz, 2002), (b) temporal precedence of process change (Kazdin & Nock, 2003), and, whenever possible, (c) experimental manipulation of processes in such a manner as to be able to draw strong inferences about the relationship between treatment and mechanism (Baron & Kenny, 1986; Kraemer et al., 2002).

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