Evaluating Scientific Research on Mediators and Mechanisms of Change in Psychotherapy

Herman Egenberg and Mari Bergum Berget

Prosjektoppgave ved det medisinske fakultet

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Abstract

Psychotherapy research is a vast field with a host of studies showing significant effect by different forms of psychotherapy on different forms of pathology. However, the mechanisms through which these effects occur are still not established in most cases. As a part of our medical education we decided with the guidance of professor Per Høglend from the University of Oslo, to critically evaluate a selection of studies attempting to establish so-called mediators in order to describe mechanisms of change in psychotherapy. We used an article by Alan E Kazdin, describing requirements and criteria for such mediation studies, as a guide for our evaluation. By doing this we learned that the field of research on mechanisms of change in psychotherapy is still young, and there is still confusion about terms, methods and statistical analysis regarding mechanisms of change. However, in our opinion, mediation studies holds potential for improving clinical practice, training and theory models.

Introduction

We decided to write our project article on psychotherapy research. We find psychiatry to be an interesting field, and we are especially interested in psychotherapy. We have found psychotherapy training to be rather scarce in the curriculum for medical students in Oslo, even though many psychiatrists and general practitioners of medicine are expected to provide different forms of psychotherapy. We wanted to learn more about psychotherapy, and particularly about scientific research on psychotherapy. We were delighted that prof. Per Høglend agreed to be our supervisor on the project article, as he is a world renowned expert on psychotherapy research. It was prof. Høglend who suggested that we use the 2007 article by Alan E Kazdin as a basis for our project article. The article describes, among other things, methods for critically evaluating certain kinds of research on psychotherapy, namely research on mechanisms of change in psychotherapy. We wanted to use the 2007 Kazdin article as a guideline, and search for and critically evaluate a selection studies. *More specifically, we wanted to evaluate whether they successfully demonstrate mechanisms of change.* By doing this we assumed that we would not only learn about some of the latest developments in psychotherapy research, but also learn something about how psychotherapy research is conducted and evaluated in general. Even though this article is largely an exercise in gathering and evaluating scientific data on complex subjects, we hope that readers will find the discussions regarding the different mediators, as well as mediator research as a whole valuable, and that the article can provide deeper understanding of the intricacies and challenges of psychotherapy research.

Innholdsfortegnelse

Chapter 1: Methods and Materials

In 2007 Alan E Kazdin published the article "Mediators and Mechanisms of Change in Psychotherapy Research". The article claims that even though there is enormous progress in psychotherapy research, we lack "an evidence-based explanation for how or why even our most well studied interventions produce change". The article provides methodological requirements for demonstrating mediators and mechanisms of change in psychotherapy. Finally, the article calls for more research to be done on mechanisms of change in psychotherapy. In this article, we will review a selection empirical studies on mechanisms of change in psychotherapy published between 2007 and 2015. We will critically evaluate the articles independently, based on Kazdin's criteria, and conclude on whether or not our selection of studies fulfils the guidelines presented in Kazdin's article from 2007.

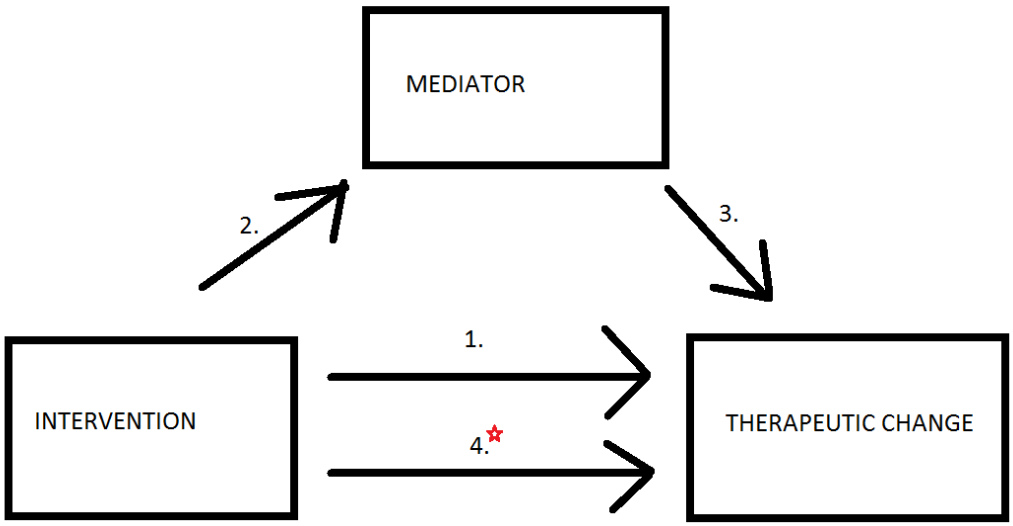
MECHANISMS OF CHANGE IN PSYCHOTHERAPY

"We know well that therapy "works," i.e., is responsible for change, but have little knowledge of why or how it works." (Kazdin, 2007) In order to discover the mechanisms of change in psychotherapy, we need an empirical method of looking at the mechanisms through which the therapy works. "To evaluate how change comes about, research often looks at mediators." (Kazdin, 2007) A **Mediator** is a construct that shows significant statistical relations between an intervention and an outcome. The intervention causes a change in the mediator, which causes a change in the outcome. *For example, when patients with depression get better after getting psychotherapy, one could assume that the change was mediated by the patient's improved self-efficacy. If that is the case, self-efficacy is a mediator between the intervention (psychotherapy) and the outcome (less symptoms of depression). Furthermore, one could assume that if the psychotherapy failed to provide the patients an improved sense of control, the outcome would not be affected, and the patients would not get better from their depression.* In many cases, psychotherapy works through several mediators, and the complete picture is complicated. Mediators cannot completely explain the mechanisms of change; they do not explain the precise process through which change comes about. However, studying mediators can be a useful first step in understanding mechanisms of change in psychotherapy.

REQUIREMENTS FOR DEMONSTRATING MEDIATORS AND MECHANISMS OF CHANGE

Kazdin states in his 2007 review that establishing a mediator or mechanism has several criteria:

- **Strong association**: there has to be a strong association between the intervention, the proposed mediator, and the therapeutic change. This association is most commonly demonstrated by multiple regression studies. In a multiple regression study, the association has to be demonstrated in four steps. Here are the steps, referred to as 1 through 4.
    1. The intervention (A) must be related to therapeutic change (C)
    2. The intervention (A) must be related to the proposed mediator (B)
    3. The proposed mediator (B) must be related to the therapeutic change (C) and
    4. The relationship between the intervention (A) and the therapeutic change (C) must be significantly reduced after statistically controlling for the proposed mediator. (B)



- **Specificity**: specificity of the association between the intervention, mediator and outcome must be demonstrated. It is always possible that multiple unknown processes are mediating the change in outcome. By including several proposed mediators in a study, as opposed to measuring just one proposed mediator, you increase specificity of proposed mediators.

- **Consistency**: observed results must be replicable across a variation of studies in order to demonstrate consistency.
- **Experimental Manipulation**: Direct manipulation through an experiment, as is often demonstrated in randomized controlled trials (RCT) will strengthen the case between cause and outcome.
- **Timeline**: The mediator should temporally precede the outcome
- **Gradient**: Showing a gradient in which a stronger activation of the proposed mediator is associated with greater change (dose-response relation) in the outcome will strengthen the case for a particular mediator. It is possible that there is no dose-response relation, but rather qualitative or on-off gradient, or that the relation is not linear.
- **Plausibility**: Finally, plausibility of an explanation of how a mediator operates is also a requirement for establishing a mediator.

RECOMMENDATIONS FOR RESEARCH BY KAZDIN

Kazdin states that little research has addressed the conditions necessary to establish mediators or mechanisms. In general, the investigation of mediators and mechanisms of therapy can be improved in the following ways:

- Use theory as a guide
- Include measures of potential mediators in treatment studies
- Establish the timeline of the proposed mediator and related change in outcome
- Assess more than one mediator
- Use design that can evaluate mediators and mechanisms of change
- Examine consistencies across different types of studies
- Intervene to change the proposed mediator

We will now critically evaluate a selection of recent research on mechanisms of change in psychotherapy to determine whether they follow Kazdin's recommendations, and whether they successfully establish mediators and mechanisms of change. Our main focus will be on evaluating the proposed mediators in each study.

CRITERIA FOR INCLUSION AND EXCLUSION

When deciding on criteria for inclusion and exclusion of articles we wanted to achieve the following:

- Articles should be attempting analysis of mediation in adult psychotherapy.
- Selection of articles should cover different proposed mediators.
- Selection of articles should cover different types of psychotherapy.
- Selection of articles should describe different study designs.

When searching for articles to review, we decided to use google scholar, rather than the PubMed search engine. We found that google scholar was a more efficient choice when searching for a small selection of relevant articles. It was helpful to use PubMed as a supplementary tool. We did five different searches, differentiating between different forms of psychotherapy. In each search we reviewed the abstracts beginning from the top of the search results. (Google Scholar sorts articles by relevance using complicated algorithms) When we found an article that fitted our criteria for inclusion, we included it in our project and went on to the next search. We decided to include two articles from the CBT search. The reason for this is that CBT is the form of psychotherapy that is most thoroughly taught to medical students in the University of Oslo, and therefore most familiar to us. The searches were:

- Motivational interviewing mediation analysis (1 article included)
- Psychodynamic therapy mediation analysis (1 article included)
- CBT mediation analysis (2 articles included)
- Mindfulness therapy mediation analysis (1 article included)
- Acceptance and commitment therapy mediation analysis. (1 article included)

Chapter 2: Results

1 THE MEDIATING ROLE OF INSIGHT FOR LONG-TERM IMPROVEMENTS IN PSYCHODYNAMIC THERAPY (Johansson, P et. al. 2010)

ABSTRACT

OBJECTIVE:

According to psychoanalytic theory, interpretation of transference leads to increased insight that again leads to improved interpersonal functioning over time. In this study, we performed a full mediational analysis to test whether insight gained during treatment mediates the long-term effects of transference interpretation in dynamic psychotherapy.

METHOD:

This study is a randomized clinical trial with a dismantling design. One hundred outpatients seeking psychotherapy for depression, anxiety, personality disorders, and interpersonal problems were randomly assigned to 1 year of weekly sessions of dynamic psychotherapy with transference interpretation or to the same type and duration of treatment with the same therapists but without the use of transference interpretation. Interpersonal functioning and insight were measured pretreatment, posttreatment, and 1 year and 3 years after treatment termination.

RESULTS:

Contrary to common expectation, patients with a life-long pattern of low quality of object relations and personality disorder pathology profited more from therapy with transference interpretation than from therapy with no transference interpretation. This long-term effect was mediated by an increase in the level of insight during treatment.

CONCLUSIONS:

Insight seems to be a key mechanism of change in dynamic psychotherapy. Our results bridge the gap between clinical theory and empirical research.

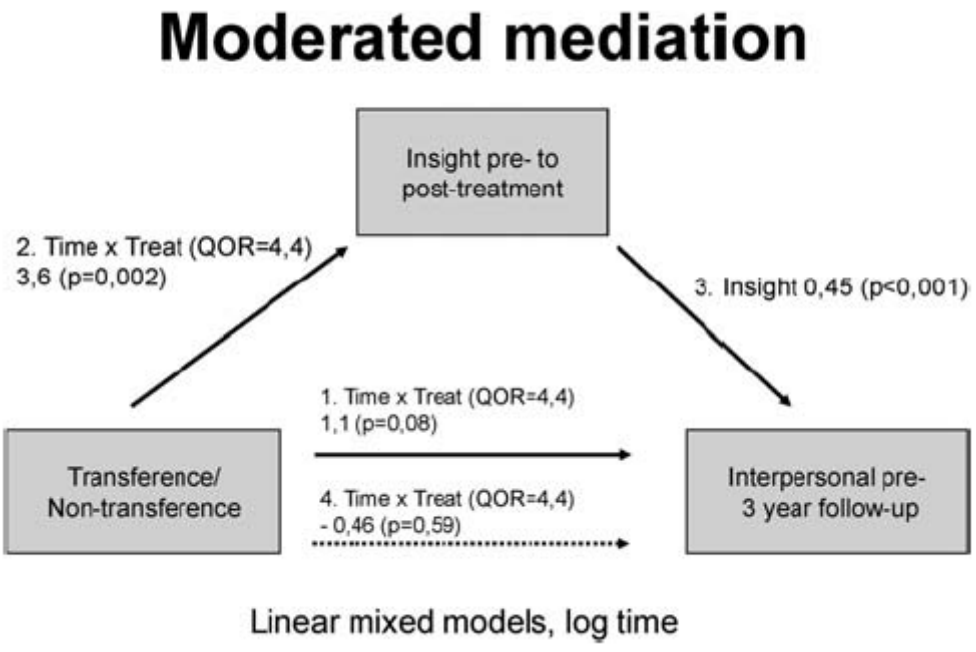
EVALUATION OF VALIDITY OF PROPOSED MEDIATOR

Introduction:

In the RCT by Paul Johansson and Per Høglend from 2012, the authors claim to show that a specific theory derived mediator (insight) explains a substantial proportion of the long term effects of transference interpretation. “Insight increased dramatically during treatment in the transference group, but did not change much during the following years, whereas interpersonal functioning continued to improve.” In this case, the intervention (transference interpretation) caused change in the proposed mediator (insight) which preceded and caused the outcome (improved interpersonal functioning).

Strong association:

In half of the patients, (those with a low quality of relations-score (QOR)) there is a significant increase in the proposed mediator (insight) from before to after treatment (path 2). In the other half, the change in insight is no different between intervention and control. In the low QOR-group, there is an association between the mediator and the outcome interpersonal functioning (path 3). “Sixty percent of the direct effect of transference interpretation on outcome variance for the typical low QOR patient was accounted for by the indirect effect of insight.” (Johansson 2010) When controlling for insight the study concluded that this group (low QOR) had weak or no direct effect of the treatment (effect of transference interpretation) (path 4). These associations could not be replicated in the group with high QOR. The statistical significance of the mediational pathway was tested by utilizing a method proposed by Holmbeck. (Holmbeck 2002)



Specificity:
Because there are no measurements of other mechanisms or proposed mediators, the study fails to account for the proposed mediator's specificity.

Consistency:
"Prior studies on the role of insight in psychodynamic therapy have shown mixed results. No studies have tested all steps of mediator methodology." (Johansson 2010) In order to demonstrate consistency with conviction, further studies should be conducted.

Experimental Manipulation:
You can argue that transference interpretation technique causes increased insight. Internal Validity is strengthened as this study is an RCT, thereby reducing risk of systematic errors such as confounding variables.

Timeline:
The study demonstrates that an increase in insight precedes an increase in interpersonal functioning measured on a 3 year follow up. However, both insight and interpersonal functioning were measured only before and after treatment. If the variables were to be measured during treatment as well, it would further strengthen the case for the proposed mediator.

Gradient:
The discovery of a strong association between mediator and outcome (in patients with low QOR, whereas there was no effect in the patients with high QOR) suggests that the effect is graded. However, since the study only measured one intervention, it is not possible to demonstrate type of gradient relation between mediator and outcome. The gradient might be dose-response related, on-off related or related in other ways.

Plausibility:
The proposed mechanism of change is firmly rooted in psychoanalytic theory. "Insight acts as a mediator (mechanism) for the long-term effects of transference interpretation." (Johansson 2010) However, the meaning of the term insight is not thoroughly agreed upon. "A central problem in psychoanalytic literature seems to be the need to define the qualities that distinguish "true" or "emotional" insight from purely "intellectual" insight. According to

some theorists, insight is only true when it is followed by therapeutic change." (Johansson 2010) This study focuses on insight acquired during transference work. "Insight gained through the therapist's interpretation of transference may be particularly valuable in that it facilitates integration of cognition and affect more effectively." (Johansson 2010) To summarize, even though the meaning of the term insight is not agreed upon by all, it is evaluated in the context of transference work, where it as a mechanism of change is central in clinical theory. By examining a well-established and plausible mechanism of change, the case for the proposed mediator is strengthened.

Discussion:

- The study demonstrated a strong association between the intervention, the proposed mediator and the outcome, and the direct association between the intervention and the outcome was reduced or eliminated when the mediator was accounted for in the analysis.
- The study also demonstrated that the change in the proposed mediator probably occurred prior to outcome on a timeline.
- The study fails to demonstrate specificity which weakens the case for the mediator.
- Further studies have to be conducted in order to demonstrate consistency and to establish the gradient relation between the mediator and the outcome.
- The mediation effect could only be demonstrated in the group with low quality of relations before the treatment took place. Therefore, this is a moderated mediation, which weakens the case for the mediator in a broader perspective.
- The selection of therapists conducting the study was a small group of seven, with above average clinical experience. This weakens external validity of the study as it makes it difficult to replicate the therapy situation in question.
- Furthermore, the therapy was manualized and monitored, which makes therapy generalization additionally problematic.

2 MECHANISMS OF CHANGE UNDERLYING THE EFFICACY OF COGNITIVE BEHAVIOUR THERAPY FOR CHRONIC FATIGUE SYNDROME IN A SPECIALIST CLINIC: A MEDIATION ANALYSIS (Stahl, D et. al. 2014)

ABSTRACT

BACKGROUND:

Several randomized controlled trials (RCTs) have shown that cognitive behavioural psychotherapy (CBT) is an efficacious treatment for chronic fatigue syndrome (CFS). However, little is known about the mechanisms by which the treatment has its effect. The aim of this study was to investigate potential mechanisms of change underlying the efficacy of CBT for CFS. We applied path analysis and introduce novel model comparison approaches to assess a theoretical CBT model that suggests that fearful cognitions will mediate the relationship between avoidance behaviour and illness outcomes (fatigue and social adjustment).

METHOD:

Data from 389 patients with CFS who received CBT in a specialist service in the UK were collected at baseline, at discharge from treatment, and at 3-, 6- and 12-month follow-ups. Path analyses were used to assess possible mediating effects. Model selection using information criteria was used to compare support for competing mediational models.

RESULTS:

Path analyses were consistent with the hypothesized model in which fear avoidance beliefs at the 3-month follow-up partially mediate the relationship between avoidance behaviour at discharge and fatigue and social adjustment respectively at 6 months.

CONCLUSIONS:

The results strengthen the validity of a theoretical model of CBT by confirming the role of cognitive and behavioural factors in CFS.

EVALUATION OF VALIDITY OF PROPOSED MEDIATOR

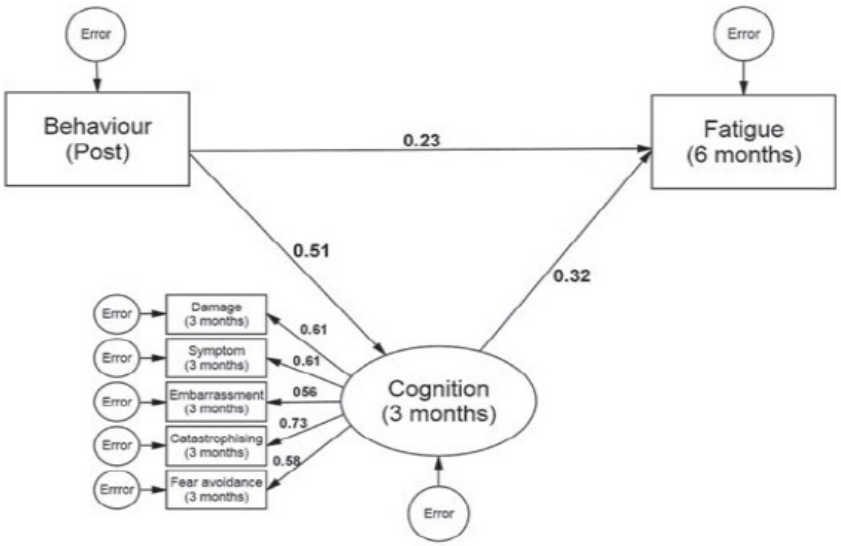
Introduction:

The cohort study by D. Stahl, K. A. Rimes and T. Chalder from 2014 claims that that the proposed mediator (cognition) can account for changes in outcome (reduced fatigue). "In this study we assessed … that fearful cognitions would at least partially mediate the relationship between change in avoidance behavior and illness outcomes (fatigue and

disability).” (Stahl 2012) Instead of using a mediation analysis pathway from intervention to outcome using multiple regression analysis, the study analyses the mediating effect between an independent variable and an outcome using path analysis. In this case cognition mediates the relationships between change in behaviour and illness outcomes. The study argues that by comparing path analysis of two different mediation pathways on a timeline, one can establish in which direction mediation occurs. “For each of the two outcome variables (fatigue and social adjustment), we compared full and partial mediation processes for two proposed pathways: behaviour → cognition → outcome and cognition → behaviour → outcome.” (Stahl 2012) The results are said to “strengthen the validity of a theoretical model of CBT by confirming the role of cognitive and behavioural factors in CFS.” (Stahl 2012).

Strong association:

The mediation analysis revealed that the proposed mediator “fear avoidance beliefs” was “positively associated with the outcome variables fatigue and social adjustment respectively.” (Path 3) A path analysis method as proposed by Mackinnon was used. (MacKinnon 2008) An association is found, as shown in the figure.



However, the criteria for establishing an association is different when doing path analysis compared to doing multiple regression analysis, and the results shown are a result of that. By using a comparison of two mediating paths instead of multiple regression analysis, the study bypasses traditional requirements for statistical strength of the proposed mediator. “The main changes in all measures occurred between baseline and discharge, with few changes

occurring afterwards, so that true causality could not be proven. However, the small changes allowed us to select the path 'behaviour → cognition → outcome' as the better mediation model." (Stahl 2012) Evaluating the association between behaviour, cognition and outcome in this manner might hold some value in understanding how CBT works for CFS patients, but as stated in the study: true causality could not be proven. In addition, sufficient statistical data for evaluating association is not provided. The tables do not seem to match the figures. There is an inexplicable difference between the data in table 3 and figure 2.

Specificity:
By attempting to establish a causality chain between behaviour and cognition, which both could be hypothesized as mediating treatment effects of CFS patients receiving CBT, the study makes a case for the specificity of the possible mediators cognition and behaviour, where they to be evaluated in further studies.

Consistency:
Prior studies on the subject have suggested that CBT effect is mediated by change in cognitive responses. "In summary, studies to date suggest that change in cognitive responses but not behavioural avoidance may mediate the effect of CBT. However, none of the studies used mediators measured before the outcomes." (Stahl 2012) There needs to be further studies that focus on mediational analysis, preferably using multiple regression studies of proposed mediators, to establish consistency for the proposed mediator.

Experimental manipulation:
The study was not a RCT, and could therefore not assess whether there was a direct manipulation of the proposed mediator during the treatment, nor if the outcome was a result of the treatment, as opposed to other factors. Furthermore, the independent variable was not treatment, but a status variable measured after treatment. This weakens internal validity of the study. Further studies using RCT as a method would reduce risk of systematic error and strengthen the case for the proposed mediator.

Timeline:
The study describes a timeline, with measurements of behaviour, cognition and both outcome variables at baseline, discharge, 3 months, 6 months, 9 months and 12 months after baseline. This allowed the study to measure which changes preceded which. However, most of the

changes took place during treatment. Therefore, establishing a mediated effect in which a significant change in the proposed mediator preceded a significant change in outcome was impossible.

Gradient:
There has been no attempt at demonstrating a gradient in which a greater activation of the proposed mediator caused an increased effect on the outcome.

Plausibility:
"In summary, studies to date suggest that change in cognitive responses but not behavioural avoidance may mediate the effect of CBT. " (Stahl 2012) "We hypothesized that, as CBT in this context focuses initially on changing avoidance behaviour, fearful cognitions will at least partially mediate the relationship between change in avoidance behaviour and illness outcomes (fatigue and disability). The current study allowed preliminary investigation of this possibility." (Stahl 2012) The statements made in the study as shown above are slightly paradoxical. Behaviour cannot both be considered as an independent variable and a mediating variable at the same time. In order to provide a truly plausible explanation for the mechanisms of change in CBT, further studies need to be conducted.

Discussion:

- The study claims to shows a statistically strong association between an independent variable, a proposed mediator and an outcome.
- The study uses a timeline in order to find out which changes in outcome and proposed mediators precede which.
- The study uses path analysis to compare two proposed mediating pathways: behaviour → cognition → outcome, and cognition → behaviour → outcome, while not evaluating a pathway including the intervention itself, for example: intervention → proposed mediators (behaviour or cognition) → outcome. Comparing pathways in this matter made a case for favouring one pathway over the other, but could not prove true causality as to how the effect of CBT is mediated.
- The attendance dropped from 389 to 183 at the follow up 12 months after treatment. The small size of the attendance rate (47%) is problematic.

3 FROM IN-SESSION BEHAVIORS TO DRINKING OUTCOMES: A CASUAL CHAIN FOR MOTIVATIONAL INTERVIEWING (Moyers, T. B. et. Al. 2009)

ABSTRACT

Client speech in favour of change within motivational interviewing sessions has been linked to treatment outcomes, but a causal chain has not yet been demonstrated. Using a sequential behavioural coding system for client speech, the authors found that, at both the session and utterance levels, specific therapist behaviours predict client change talk. Further, a direct link from change talk to drinking outcomes was observed, and support was found for a mediational role for change talk between therapist behaviour and client drinking outcomes. These data provide preliminary support for the proposed causal chain indicating that client speech within treatment sessions can be influenced by therapists, who can employ this influence to improve outcomes. Selective eliciting and reinforcement of change talk is proposed as a specific active ingredient of motivational interviewing.

Theresa B. Moyers, Tim Martin, Jon M. Houck, Paulette J. Christopher, and J. Scott Tonigan, 2009

EVALUATION OF VALIDITY OF PROPOSED MEDIATOR

Introduction:

In this study by Moyers and others, a proposed mediator, change talk during motivational interview, is claimed to mediate the effect between motivational interview consistent behaviour (MICO) and an outcome, drinks per week after 5 weeks. The data included videotapes from motivational interview (MI) treatment sessions. The videotapes from the MI treatment sessions were examined to find motivational interview consistent behaviour, (MICO) motivational interview inconsistent behaviour, (MIIC) and patient change talk. Drinking outcomes were measured at subsequent follow-ups up to 5 weeks after the treatment session. "We hypothesized that if MI were rendered effective by therapists' elicitation of client change talk, the probability of change talk in these MET sessions would be greater when therapists used behaviours prescribed in MI. Furthermore, we hypothesized that the change talk that occurred in these MET sessions should be associated with improved substance abuse outcomes." (Moyers 2009)

Strong association:

In this study, the proposed mediator is patient change talk. The study finds a correlation between MICO and the proposed mediator (path 2). The study also measures the correlation between the proposed mediator and the therapeutic change, drinks per week 5 weeks after the therapy session. (Path 3) There is an association but as stated in the article, the association is relatively small. “The data indicate a relatively brief and relatively small association between change talk during MI sessions and drinking outcomes.” (Moyers 2009) “Within this sample, change talk appears to mediate between MICO and drinking outcomes and accounted for about 30% of the effect.” (Moyers 2009) However, when evaluating a second mediator in the test, counter change talk, the results could not be replicated with significance. To calculate the association the study uses a method that “is conceptually similar to the model described by Baron and Kenny” This method is described by Mackinnon. (Mackinnon 2008) There were certain alterations when calculating confidence intervals in which they used a method proposed by Mackinnon and others (Mackinnon 2007) Furthermore, while 30% of the effect of the intervention could be attributed to the proposed mediator, the total effect of the intervention was only 3%. (path 1)

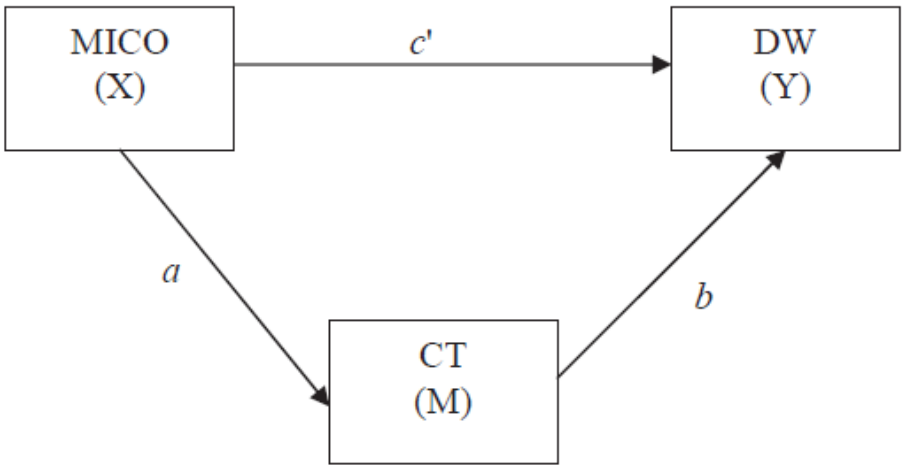


Figure 1. Mediation model illustrating the independent variable, motivational interviewing consistent behaviors (MICO); the mediator, change talk (CT); and the dependent variable, drinks per week (DW). Relationships between variables are represented as *a,* the relationship between X and M; *b,* the relationship between M and Y; and *c′*, the relationship between X and Y adjusted for the effects of M.

Specificity:

When change talk is considered as a sole mediator in a statistical analysis, the association is strong, but when both change talk and counter change talk is evaluated as mediators between MICO and drinking outcome, statistical significance is lost. This result shows that the specificity of the proposed mediator is questionable, and weakens the case for the proposed mediator. Specificity might have been difficult to demonstrate due to the "striking amount of ambivalence (back and forthness) in client speech, even when change talk was offered... Change talk, although predictive of better outcomes, occurred nearly simultaneously with counterchange talk. This was so common that our coders learned to listen for a "change talk sandwich," an utterance of change talk surrounded by two instances of counterchange talk ("I don't need to change my drinking. Well, I mean, I need to cut down for sure, but no way am I problem drinker like they say I am."). Furthermore, both MICO and MIIN were associated with an increased probability of counterchange talk." (Moyers 2009) The problem such ambivalence and complexity of patient talk poses for mediator specificity should be addressed in further studies.

Consistency:

"Empirical evidence to support the claim that client speech is an active ingredient in MI is sparse but growing, with most attention being paid to the second component of the chain: the relationship between change talk and client outcomes. In general, this research shows a consistent relationship between client language that occurs during an MI session and subsequent desirable behaviour change." (Moyers 2009) However, "there has not been a study that examines all elements of a mediational model within a single intervention." (Moyers 2009) To establish consistency for the proposed mediator, further studies have to be conducted.

Experimental Manipulation:

The study does not provide an experimental manipulation of change talk in a RCT. Therefore the association between intervention, mediator and outcome could possibly be explained by other unknown variables or reverse causality. A RCT in which patient change talk is directly manipulated would strengthen the case for the proposed mediator. "A stronger argument for the causal nature of change talk can be made only via experimental studies" (Moyers 2009).

Timeline:

As a result of this study method, there is an obvious timeline where the proposed mediator occurs before the therapeutic change. Additionally, outcome is measured repeatedly on a 5 week timeline. This strengthens the case for the proposed mediator. However, the intervention and mediator occur intermittently during a single session. By applying such a timeline, the study cannot prove that therapist behaviour only affects patient change talk, and not the other way around. To strengthen the case for the proposed mediator in further studies, this issue should be addressed.

Gradient:

The study shows a gradient in the relationship between patient change talk and drinks per week, which strengthens the case for the proposed mediator. However, the nature of the study cannot prove that other factors are not causing this effect. In order to establish the gradient relationship more convincingly, studies of more experimental nature should be conducted.

Plausibility:

Client speech is an important part of clinical theory of motivational interviewing. "Since the inception of MI, client speech has been hypothesized as a critical component of such interventions." (Moyers 2009) "Theory states that "therapists should attempt to elicit language in favour of change" (Moyers 2009) by exploring mechanisms of change which is rooted in established theory, plausibility of the proposed mediator is strengthened.

Discussion:

- The total effect of the mediator on the outcome was only 1%. (The mediator stood for 30% of the total effect, but the effect was only 3%.) The conceptual validity of the proposed mediator is therefore questionable. Where further studies to describe a stronger effect between the therapy method and the outcome, a stronger case for the mediator could be made.
- In order to strengthen the case for the proposed mediator, research should address the disagreements regarding the mediator's measurement. "There is some disagreement about the type of client speech that is most important (change talk vs. commitment language) and the way it is measured (frequency vs. strength)" (Moyers 2009)

- The lack of experimental manipulation of the proposed mediator, for example by means of RCT study design, weakens the case for the proposed mediator.
- The mediation effect of change talk could not be significantly established when you added counter-change talk as an additional mediator. Although plausible explanations where offered, the reasons for the lack of association when measuring multiple mediators could not be satisfactory explained in the study. This weakens the case for the proposed mediator, especially because it undermines mediator specificity.
- Additionally, the study does not account for a second session of therapy that took place, because the data from these sessions were never analysed.
- It could have been fruitful to calculate reverse causality between the proposed mediator and MICO, as well as reverse causality between Drinks per Week and Change Talk. It is not unfathomable that an already made decision to drink less in the future will lead to increased change talk which again leads to increased MICO by the therapist. If the researchers were to conduct an RCT, the problem with reversed causality could be reduced.
- The study suggests future use of mediation analysis when training therapists in the motivational interview technique. The case for the proposed mediator might not be particularly strong, but the study both provides methods for inducing the proposed mediator in therapy, as well as indicating what clinicians ought not to do, if they wish to increase frequency of proposed mediator. This demonstrates some of the value of mediation studies. If mediators can be established with conviction, it can provide great assistance in improving efficiency of psychotherapy.

4 PSYCHOLOGICAL FLEXIBILITY AS A MEDIATOR OF IMPROVEMENT IN ACCEPTANCE AND COMMITMENT THERAPY FOR PATIENTS WITH CHRONIC PAIN FOLLOWING WHIPLASH (Wicksell, R et. al. 2010)

ABSTRACT

Cognitive behavior therapy (CBT) has made important contributions to chronic pain management, but the process by which it is effective is not clear. Recently, strong arguments have been raised concerning the need for theory driven research to e.g. identify mechanisms of change in CBT and enhance the effective- ness of this type of treatment. However, the number of studies addressing these issues is still relatively scarce. Furthermore, the arrival of varieties of CBT with seemingly different process targets increases the need for such information. The present study explored the processes of change in a previously reported successful randomized controlled trial evaluating the effectiveness of an exposure-based form of behavioral and cognitive therapy, Acceptance and Commitment Therapy (ACT), on improvement in pain-related disability and life satisfaction for patients suffering from whiplash-associated disorder (WAD). Several process variables relevant to theories underlying traditional CBT were included: pain, distress, kinesiophobia, self-efficacy, and the process primarily targeted by ACT: psychological inflexibility. Mediation analyses were performed using a non-parametric cross-product of the coefficients approach. Results illustrated that pain intensity, anxiety, depression, kinesiophobia, and self-efficacy did not have significant mediating effects on the dependent variables. In contrast, significant indirect effects were seen for psychological inflexibility on pain-related disability (pre- to post-change scores) and life satisfaction (pre- to post; pre- to 4-month follow-up change scores). Although tentative, these results support the mediating role of psychological inflexibility in ACT-oriented interventions aimed at improving functioning and life satisfaction in people with chronic pain.

EVALUATION OF VALIDITY OF PROPOSED MEDIATOR

Introduction:

This study by Rikard K. Wicksell et al. (2010) investigates if the improvements in the primary outcomes disability and life satisfaction were obtained through changes in the primary mediator psychological inflexibility, by using the intervention Acceptance and Commitment Therapy (ACT) in patients suffering from chronic pain following whiplash. The study is based on data set from an ACT-based RCT by Wicksell et al. (2008), where the

intervention group had 10 ACT sessions of 60 minutes during an eight week period. The authors claim that "the improvements in outcome seen in this RCT were obtained through theoretically targeted changes in psychological inflexibility" (Wicksell, 2010). The present study also investigated the mechanism of effect of the hypothesized mediators pain intensity, anxiety, depression, kinesophobia and self-efficacy. "Pain or distress did not bear a significant functional relation to disability and life satisfaction outcomes in this data set, indicating that the improvements seen were not mainly accomplished through such symptom alleviation. Similarly, neither reduced kinesiophobia nor improved self-efficacy appeared to be relevant mediating variables" (Wicksell, 2010).

Strong association:

Patients in the ACT group improved significantly in both outcome measures pain-related disability (PDI) and life satisfaction (SWLS). The control group, which received treatment as usual (TAU), had increased pain-related disability, and less satisfaction with life. ACT was significantly related to therapeutic change in all outcome measures (path 1). The ACT group had statistically higher primary mediator, psychological flexibility, measured by PIPS-total score, PIPS-avoidance score and PIPS-fusion score, and also kinesiophobia and depression (HAD-d) of the secondary mediators (path 2).

Psychological inflexibility, measured by PIPS-total score, was related to outcome change in life satisfaction (SWLS) both pre to four months follow-up (p=.018) and pre to post (p=.009). (Path 3) PIPS-total score was not related to outcome on pain-related disability (PDI) (path 3). When measured as PIPS-fusion score, the mediator was related to treatment effect on pain-related disability pre to post and life satisfaction. There were no significant mediation effects of the proposed secondary mediators, pain, anxiety, depression, kinesiophobia or self-efficacy, on pre- to post-changes or pre- to follow-up changes in pain-related disability (PDI) or life satisfaction (SWLS) (path 3).

When controlling for the effect of psychological flexibility (path 4), the relation between ACT and the therapeutic change was no longer significant in all outcome measures, except life satisfaction pre to post.

The only strong association in this study is between the intervention, the proposed mediator psychological flexibility measured by PIPS-total score and SWLS pre- to four-month follow

up as outcome measure. The interpretation of this finding is unclear, because psychological inflexibility is only measured as post-treatment score. The mediator may be altered by treatment, but impossible to say because of lack of pre-treatment score. In this study, 120 tests were performed to prove specificity. 20 of these were tests involving psychological flexibility as measured by PIPS-total score. This increases the risk of type 1 errors.

Specificity:

Psychological flexibility is the proposed primary mediator, because this is the process primarily targeted by ACT, but this study also investigates five hypothesized secondary mediators. This increases the specificity of the proposed mediator, but there may still be unknown processes mediating the change in outcome which needs to be addressed in future studies.

Consistency:

”The present study is the first to apply formal mediation analysis to examining the effects of an ACT RCT for chronic pain” (Wicksell 2010). Therefore no consistency is demonstrated.

Experimental Manipulation:

The study is based on a RCT (Wicksell, 2008), which strengthens the case for the proposed mediator because the change in mediator can be interpreted as a causal effect of the treatment.

Timeline:

For outcome measures (PDI and SWLS) two different change scores were calculated, pre- to post-assessment scores and pre- to 4-month follow-up scores. Post-assessment scores were used for the hypothesized mediators. The study argues that use of post-assessment scores in the analyses of the mediators is not a weakness because of lack of pre-assessment differences between the groups. When change-scores are not used for measurement of mediators, it is not possible draw conclusions of the correlation with treatment. Because the variables are not measured during treatment, this study has an incomplete timeline.

Gradient:

There has been no attempt to demonstrate a gradient in which a greater activation of the proposed mediator caused an increased effect on the outcome.

Plausibility:

In ACT-treatment the main target is to increase psychological flexibility to improve functioning and quality of life. "ACT is explicitly not aimed at reducing pain or distress, or at changing the frequency or content of thoughts. Instead, it promotes greater acceptance of negative private experiences in order to increase psychological flexibility. Several treatment evaluations have suggested the utility of an ACT-oriented approach for chronic pain" (Wicksell et al., 2010). The choice of treatment and mediator in this study is plausible.

Discussion:

- A weakness of this study is that they performed a total of 120 statistical analyses on only 20 patients. 20 of these were statistical analyses of PIPS-total score. A significance-level at $p < .05$ is liberal when this many tests were performed. The authors did not use Bonferoni-adjusted significance level. This increases the risk of type 1 errors. In our opinion statistical validity is totally compromised.
- Another important weakness of this study is the lack of change-scores as measurement of proposed mediators. When change-scores are not used for measurement of mediators, it is not possible to draw firm conclusions of the correlation with treatment.
- The study claims to show significant indirect effects for psychological inflexibility (PIPS) on life satisfaction pre- to follow-up change scores. The other hypothesized mediator variables did not show any significant relation to disability and life satisfaction outcomes.
- Small study, only 20 patients completed the study (including 11 in the treatment condition), "the findings should be considered tentative both given the relatively small sample size and the particular patient group included. Consequently, replication of these findings is important and larger scale studies would help ascertain the stability and generalizability of these results" (Wicksell 2010).
- A weakness of this study is comparing ACT-treatment to "treatment as usual" (TAU), because there is no knowledge of what this treatment consists of. In this study, the control group had increased pain-severity after treatment.
- This is the first study investigating mediators of change in ACT for patients with chronic pain following whiplash. There is a need of further studies with larger patient

groups to show consistency and plausibility, and to explore unknown mediating processes.

5 WHICH COGNITIONS AND BEHAVIOURS MEDIATE THE POSITIVE EFFECT OF COGNITIVE BEHAVIOURAL THERAPY ON FATIGUE IN PATIENTS WITH MULTIPLE SCLEROSIS? (Knoop, H. et. al. 2012)

ABSTRACT

Background Chronic fatigue is a common symptom of multiple sclerosis (MS). A randomized controlled trial (RCT) showed that cognitive behavioural therapy (CBT) was more effective in reducing MS fatigue than relaxation training (RT). The aim of the current study was to analyse additional data from this trial to determine whether (1) CBT compared to RT leads to significantly greater changes in cognitions and behaviours hypothesized to perpetuate MS fatigue; (2) changes in these variables mediate the effect of CBT on MS fatigue; and (3) these mediation effects are independent of changes in mood.

Method Seventy patients (CBT, n=35; RT, n=35) completed the Cognitive and Behavioural Responses to Symptoms Questionnaire (CBSQ), the Brief Illness Perception Questionnaire (B-IPQ) modified to measure negative representations of fatigue, the Hospital Anxiety and Depression Scale (HADS), and the Chalder Fatigue Questionnaire (CFQ), pre- and post-therapy. Multiple mediation analysis was used to determine which variables mediated the change in fatigue.

Results Avoidance behaviour and three cognitive variables (symptom focusing, believing symptoms are a sign of damage and a negative representation of fatigue) improved significantly more in the CBT than the RT group. Mediation analysis showed that changing negative representations of fatigue mediated the decrease in severity of fatigue. Change in anxiety covaried with reduction in fatigue but the mediation effect for negative representations of fatigue remained when controlling for improvements in mood.
Conclusions Change in beliefs about fatigue play a crucial role in CBT for MS fatigue. These beliefs and the role of anxiety deserve more attention in the further development of this intervention.

H. Knoop, K. van Kessel and R. Moss-Morris, 2011

EVALUATION OF VALIDITY OF PROPOSED MEDIATOR

Introduction:

In this study by Knoop et al. (2011), the authors claim to show that in patients with multiple sclerosis, the outcome reduced fatigue is mediated by change in negative perceptions of fatigue by using the intervention cognitive behavioural therapy (CBT). In the present study, they also investigated the proposed mediators avoidance behavior, symptom focusing and believing symptoms are a sign of damage. The data set used in this study is collected from a previous RCT (van Kessel et al., 2008) where the intervention group received eight weekly individual sessions of CBT by one therapist, and the control group received eight individual sessions of relaxation training (RT).

Strong association:

In the RCT (van Kessel et al., 2008), "both CBT and RT had a positive effect on the level of fatigue and related disability. However, in the CBT group the level of fatigue decreased significantly more directly following treatment…. The effects of treatment were maintained at follow-up, 6 months later" (Knoop et al., 2011). This illustrates that the intervention is related to therapeutic change (path 1).

In this study, multiple regression was used to demonstrate the association between the intervention, the proposed mediator and the therapeutic change. CBT compared to RT gave greater positive changes in the proposed mediators, except for one (sleep) directly following treatment. Four out of eight variables were statistically significant (Bonferoni-adjusted significance level $p < .007$); CBSQ resting/avoidance of activity, symptom focusing, damaging beliefs and B-IPQ Perception of fatigue (path 2).

When analyzing the direct effect of proposed mediators on change in fatigue, only the change in the negative perceptions of fatigue (B-IPQ) significantly mediated the change in fatigue brought on by CBT (path 3). Change in the negative perception of fatigue also mediated the effect of CBT when the effects of reduction in anxiety and depression were taken into account. The significance of the indirect effect of CBT on fatigue through the proposed mediator (path 1 x 2) was tested by using bootstrapping. The 95% CI of estimated indirect effect did not include zero (-2.98 to -0.48), this shows a significant association between treatment and mediator. When correcting for the change mediated by change in the negative

perceptions of fatigue, the direct effect of CBT on the change in fatigue was no longer significant (path 4).

Specificity:

This study included eight proposed mediators, none of these were suggested as primary mediators. Four out of the eight proposed mediators were significantly reduced by the intervention; avoidance of fear, symptom focusing, damaging beliefs and perception of fatigue. The authors claim to have found that "a change in the negative representation of fatigue plays a crucial role in reduction of fatigue in MS after CBT" (Knoop et al., 2011) by demonstrating the four steps stated by Kazdin. By including other proposed mediators in the study, the specificity of change in the negative representation of fatigue as a proposed mediator is increased.

Consistency:

The present study is the first to investigate the mechanisms of change of CBT for MS fatigue. There have been three previous mediation analyses to study mechanisms of change in behavioral interventions for patients with chronic fatigue. "These studies found that, in patients with CFS, it was not the increase in physical activity or fitness but a change in cognitions that mediated the positive effect of both CBT and graded exercise therapy (GET) on the level of fatigue" (Knoop 2012). This supports the findings in this study. Changing unhelpful cognitions about fatigue needs to be a key ingredient in future interventions for fatigue.

Experimental Manipulation:

The data-set is collected from an RCT, which strengthens the case for the proposed mediator because the change in mediator can be interpreted as a causal effect of the treatment.

Timeline:

The proposed mediators and the outcome variables were measured simultaneously, pre- and post-therapy. Because mediators were not measured during treatment, this study has an incomplete timeline. A study where mediators are measured during treatment is necessary to draw firmer conclusions about an assumed causal relationship between the change in fatigue-related cognitions and the reduction in fatigue. In the RCT this study is based on, the effects

of treatment on fatigue were maintained at 6-month follow-up. These results are surprisingly not included in the present study.

Gradient:
The present study does not show that a stronger activation of the proposed mediator is associated with greater change in the outcome.

Plausibility:
"A cognitive behavioral model of MS fatigue has been formulated in which the primary disease factors, inflammation and demyelination, trigger the fatigue. Cognitive, behavioral and emotional responses worsen or perpetuate the fatigue" (Knoop et al. 2011). Based on this, and that CBT aimed at altering unhelpful cognitions and behaviors has been shown effective in reducing fatigue in chronic fatigue syndrome (CFS) and cancer survivors, a CBT intervention based on the model of MS fatigue was developed (van Kessel et al. 2008). This CBT consists of six elements, one of these elements addresses changing unhelpful cognitions surrounding MS and fatigue. The chosen intervention in this study is theoretically relevant and plausible to improve the proposed mediators and outcome.

Discussion:

- Despite the fact that CBT and RT have common elements, the present study shows a difference in outcome. In the CBT group the level of fatigue decreased significantly more. Therefore, the difference in outcome between the two treatments must be what is mediated.
- There is only one therapist in this study, which limits external validity. The results in this study may not be replicable.
- A weakness of this study is lack of one or two primary proposed mediators.
- 70 patients completed treatment, which is a good study size. The statistical analyses are satisfactorily completed; Bonferoni-adjusted significance level was used when analyzing change-scores for the proposed mediators across groups.
- This study is based on self-reported measures, in future studies more objective research methods should be applied.
- Several proposed mediators were measured which improves specificity.
- In order to firmly establish the proposed mediator, further studies should be conducted where timeline and gradient issues are secured.

6 HOW DOES MINDFULNESS-BASED COGNITIVE THERAPY WORK? (Kuyken, W. et. Al. 2010)

ABSTRACT

Mindfulness-based cognitive therapy (MBCT) is an efficacious psychosocial intervention for recurrent depression (Kuyken et al., 2008; Ma & Teasdale, 2004; Teasdale et al., 2000). To date, no compelling research addresses MBCT's mechanisms of change. This study determines whether MBCT's treatment effects are mediated by enhancement of mindfulness and self-compassion across treatment, and/or by alterations in post-treatment cognitive reactivity. The study was embedded in a randomized controlled trial comparing MBCT with maintenance antidepressants (mADM) with 15-month follow-up (Kuyken et al., 2008). Mindfulness and self-compassion were assessed before and after MBCT treatment (or at equivalent time points in the mADM group). Post-treatment reactivity was assessed one month after the MBCT group sessions or at the equivalent time point in the mADM group. One hundred and twenty-three patients with 3 prior depressive episodes, and successfully treated with antidepressants, were randomized either to mADM or MBCT. The MBCT arm involved participation in MBCT, a group-based psychosocial intervention that teaches mindfulness skills, and discontinuation of ADM. The mADM arm involved maintenance on a therapeutic ADM dose for the duration of follow-up. Interviewer-administered outcome measures assessed depressive symptoms and relapse/recurrence across 15-month follow-up. Mindfulness and self-compassion were measured using self-report questionnaire. Cognitive reactivity was operationalized as change in depressive thinking during a laboratory mood induction.

MBCT's effects were mediated by enhancement of mindfulness and self-compassion across treatment. MBCT also changed the nature of the relationship between post-treatment cognitive reactivity and outcome. Greater reactivity predicted worse outcome for mADM participants but this relationship was not evident in the MBCT group.

MBCT's treatment effects are mediated by augmented self-compassion and mindfulness, along with a decoupling of the relationship between reactivity of depressive thinking and poor outcome. This decoupling is associated with the cultivation of self-compassion across treatment.

Willem Kuyken, Ed Watkins, Emily Holden, Kat White, Rod S. Taylor, Sarah Byford, Alison Evans, Sholto Radford, John D. Teasdale, Tim Dalgleish, 2010

EVALUATION OF VALIDITY OF PROPOSED MEDIATOR

Introduction:

In this study by Kuyken et al. (2010) they search to identify mediators of mindfulness-based cognitive therapy (MBCT), and its effects for the prevention of depressive relapse/recurrence. The hypothesized mediators are mindfulness, self-compassion and cognitive reactivity. The data set in the present study is based on a RCT (Kuyken et al., 2008) that compares the effects of MBCT versus maintenance antidepressants (mADM) on the outcome. The patients were followed up at 3 monthly intervals for 15 months.

Strong association:

This study does not use change-score but compares post-MBCT data to illustrate path 1.At post-MBCT there was a significant overall effect of treatment on severity of depression, measured by HRDS scores, in the treatment groups (p=.03). This effect was no longer significant at 15-month follow-up (p=.22). There was no significant effect of treatment on relapse at 15-months follow-up (p=.55). In the cognitive reactivity sub-sample group, there is no treatment effect on either depression severity (p=.18) or relapse (p=.32). There is no difference in outcome (severity of depression and relapse) between the MBCT-group and mADM group at 15-month follow up.

The intervention significantly improved the proposed mediators mindfulness (KIMS) and self-compassion (SCS) more from baseline to post-MBCT in the MBCT group (path 2). The MBCT patients showed higher cognitive reactivity than the mADM group (path 2), but the importance of cognitive reactivity is hard to evaluate when there is no difference in outcome at 15-month follow between treatment groups. There is no effect of mediation on outcome at 15-month follow up because path 3 is not significant. This mediation study is incomplete in several of the presented analyses, and it does not present statistical information about path 4.

Specificity:

This study included three proposed mediators, none of these were presented as primary mediator. Because of incomplete mediation analyses, the study fails to demonstrate an association between intervention, mediator and outcome. There is a need of further studies to satisfactorily examine the proposed mediators, and other potential mechanisms of change.

Consistency:
This is the first study of what mediates the effect of MBCT treatment, therefore no consistency is shown.

Experimental Manipulation:
This study does provide an experimental manipulation of treatment, which strengthens the case for the proposed mediator because the change in mediator can be interpreted as a causal effect of the treatment.

Timeline:
Changes in self-compassion and mindfulness skills were measures baseline and post-MBCT (1 month after the end of MBCT, or the equivalent time in the control group). Cognitive reactivity was measured post-MBCT only. Outcome variable severity of depression was measured at 15-month follow-up. Time to depressive relapse/recurrence was measured up to the 15-month follow-up. Because the variables are not measured during treatment, this study has an incomplete timeline.

Gradient:
There is no attempt to show that greater activation of the proposed mediator is associated with greater change in the outcome.

Plausibility:
"MBCT was developed from translational research into mechanisms of depressive relapse/recurrence. MBCT´s theoretical premise is that depressive relapse is associated with the reinstatement of negative modes of thinking and feeling that contribute to depressive relapse and recurrence…. MBCT targets cognitive reactivation. Mindfulness skills are taught as a means to note distressing thoughts and feelings, hold such experiences in awareness, and cultivate acceptance and self-compassion so as to break up associative networks and offset the risk of relapse" (Kuyken et al. 2010). The chosen intervention in this study is theoretically relevant to improve outcome. In this study the MBCT patients showed higher cognitive reactivity than the mADM group, so this explanation does not seem plausible. MBCT significantly improved the proposed mediators mindfulness (KIMS) and self-compassion (SCS), these mediators are more plausible.

Discussion:

- At post-MBCT there was a significant difference in outcome between MBCT and mADM on severity of depression, measured by HRDS scores. The study does not say if the mediator was the cause of this effect, statistical analysis of path 3 or 4 on pre- to post-MBCT data is not presented.
- The proposed mediators improve in the MBCT group, but since there is no difference in outcome between MBCT and mADM treatment at 15 months follow-up, the proposed mediators should perhaps be called predictors or intermediate variables than mediators.
- This is an incomplete mediation analysis that fails to present important statistical data. The study is unsystematically presented, and difficult to interpret. This study only shows that MBCT does not make the patient´s symptoms worse. If this was a non-experimental or single-group study, it would give a clue that MBCT-treatment gives increased mindfulness skills and self-compassion that will prevent relapse post-treatment.

Chapter 3: Conclusion

In our review of 6 published mediation analysis articles we have tried to evaluate whether the individual studies make compelling cases for the establishment of the proposed mediators. We have done so by applying Kazdin's criteria for evaluation of mediation research (2007). The research we found in our search was of varying quality, and the proposed mediators were established with varying conviction.

Finishing points:

- None of the studies could establish a mediator firmly by being in concordance with all of Kazdin's criteria. It seems to date that demonstrating consistency and gradient is especially challenging.
- The stronger studies (Johansson; Knoop) excel by having superior study designs. It is clear that when conducting a mediation analysis, data should be collected and study conducted with that purpose firmly in mind. Using old data from studies conducted for other purposes seem less convincing.
- The timeline criterion was not convincingly demonstrated in any of the studies, even though it would be relatively easy to do so. Only Johansson's study demonstrated some support for a timeline for the proposed mediator.
- None of the studies demonstrated gradient. Future research should attempt to demonstrate a gradient in which a greater activation of the proposed mediator causes an increased effect on the outcome.
- Only one of the studies (Knoop) managed to sufficiently demonstrate mediator specificity. Further research should make a stronger effort to include several proposed mediators in order to make a stronger case for future mediators.
- Mediator analysis may hold significant potential for improving treatment models, training and theory.

Weaknesses of our article:

- Due to time constraints, we could not delve in to the literature to discuss if consistency of proposed mediators has been demonstrated in later studies.
- Kazdin's criteria for evaluating mediation analysis lack certain elements. We have not thoroughly evaluated studies': 1) external validity, (generalizability of therapists and

therapeutic method.) 2) type 1 and type 2 errors and 3) the use of standardized and validated measurement methods. Implementing these aspects would have strengthened our evaluation of the selection of studies. Internal validity has been evaluated to some degree, but Kazdin's criteria do not encompass all aspects of internal validity specific to different study designs.

- In our article we have used the same criteria to critically evaluate studies of different study designs. This was useful because we primarily wanted to look at the proposed mediators, not the studies as a whole. However, adding critical evaluation of the studies based on study design would have strengthened the article.
- By deciding to evaluate mediator studies on different types of psychotherapy, with different study designs looking at different mediators and different patient populations, we got a selection of studies suitable for introducing us to the field of psychotherapy research, including a plethora of terms, methods and statistical analysis in mediation research. However, by selecting such a broad range of topics, we could not delve as deeply into each mediator as we might have hoped, and were constricted to evaluating single studies regarding each mediator.
- Our method of searching for relevant studies, and our criteria for inclusion and exclusion of articles did provide us with relevant articles to evaluate, but could not give us a clear picture of all the latest research on mechanisms of change in psychotherapy. Our project article does not claim to say anything about the general status of scientific research on psychotherapy.
- We used google scholar when searching for relevant articles. Google sorts search results by relevance using complex algorithms that might change over time. This weakens replicability of the searches.

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