Treatment Effectiveness for Borderline Personality Disorder

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The Diagnostic and Statistical Manual of Mental Disorders-5 (DSM-5) Borderline Personality Disorder (BPD) diagnosis is based on nine criteria, such as feelings of emptiness, affective instability, suicidality and difficulties controlling anger. The estimated prevalence is 1.1% in the Netherlands, 2.7% in the United States and 0.7% in Great Britain. In addition, comorbidity with other disorders is high, and a staggering 75% of BPD patients attempt suicide at least once in their life, and 10% of patients actually commit suicide.

Keywords: Borderline Personality Disorder ; psychotherapy ; treatments effectiveness

1. Introduction

BPD was historically viewed as a difficult-to-treat or even untreatable disorder ^[1], but in the last 30 years this view has drastically and positively changed. Moreover, although BPD treatments are associated with high dropout rates, this might not be as high as previously assumed ^[2]. The present meta-analysis will summarize the treatment outcomes of psychological treatments (not pharmacological treatments) for BPD.

There are many non-specialized psychological treatments available, but four psychological treatments have been specifically developed for BPD (i.e., the Big-4): Dialectical Behavior Therapy (DBT), Schema Therapy (ST), Transference Focused Psychotherapy (TFP) and Mentalization-Based Treatment (MBT). Unfortunately, it is difficult to gain more insight into the relative effectiveness of these treatments because of several reasons. First, existing mutual comparisons of these so-called Big-4 psychotherapies for BPD often are inadequately powered and are, therefore, far from conclusive, e.g., [3] ^[4]. Second, as so many treatments are available, it is virtually impossible to mutually compare all existing treatments to each other in well powered randomized controlled trials (RCTs), let alone to replicate such trials. The lack of RCTs has forced previous meta-analyses to investigate BPD treatments (specialized and non-specialized) together as a group, finding superiority of specialized treatments compared to control conditions (q = 0.32) ^[5] and superiority of BPD treatments compared to treatment-as-usual (TAU; d = 0.59) ^[G] in reducing BPD severity. This is in line with findings of a recent meta-analysis ^[2], which found that psychotherapies compared to TAU were superior in reducing general BPD severity (d = 0.52), self-harm (d = 0.32) and suicide-related outcomes (d = 0.34). Direct comparisons between specific specialized treatments and TAU suggested the superiority of DBT in reducing BPD severity (d = 0.60) and self-harm (d =0.28), and the superiority of MBT compared to TAU in reducing self-harm (RR = 0.62) and suicidality (RR = 0.10). Although this meta-analysis demonstrates that it is possible to compare at least some treatments, the evidence for these effects remains limited due to the low number of direct comparisons between treatments [7]. As a result, it is difficult for patients, therapists, policy makers and researchers to estimate the efficacy of specific BPD treatments based on traditional meta-analyses of direct comparisons.

In addition, there are many aspects to these treatments and many study characteristics that can also play an important role in determining effectiveness. However, the sheer number of these aspects makes it impossible to study each in combination with all other factors in RCTs. These important treatment factors are treatment format [8![9!10]] and setting [11], but also treatment duration. There is a lot of heterogeneity in treatment duration, and even though it was suggested that treatment duration is not related to treatment outcomes [5], it is an important factor to include because there might be a dose–response relationship. Furthermore, patient characteristics such as comorbidity, age, gender and substance abuse [3![12![13![14![15![16]]]] could be important. Additionally, interesting study characteristics are trial type and study quality [17] and the handling of missing data. Lastly, publication year might be interesting to study, as one would expect that the effectiveness of treatments has increased given the radical change over the last decades in how BPD is viewed and in the development of new treatment models.

The meta-analytic approach that maximizes internal validity is examining the between-treatment effects of RCTs [18]. However, while continuing to pursue experimental comparisons of BPD treatments and predictors of treatment outcomes, different meta-analytic approaches may also shed light on this issue and help broaden our scope. Instead of metaanalyzing the effect sizes representing the difference between two study arms in an RCT, we therefore meta-analyzed the effect sizes representing the change on BPD indices within study arms. This approach offers several advantages. First, it still allows comparisons between treatment approaches and other predictors across studies. In fact, it even allows for comparisons between treatments and certain predictors that cannot be made based on traditional meta-analyses. While traditional meta-analyses are restricted by the number of studies that are available for certain comparisons, this approach can estimate effects based on a specified model and will thus be able to include more data. Second, by employing a multilevel meta-analytic approach, we can include multiple indices of BPD-pathology. Third, and perhaps most important, it allows the inclusion of the large number of uncontrolled studies that characterize the BPD treatment literature. This offers the opportunity to statistically summarize the many studies available, while not being restricted by a specific study design. Effectiveness studies of other designs are often conducted in clinical routine mental healthcare settings, an important point also raised by other authors [12]. Therefore, while the inclusion of non-RCT designs will decrease internal validity, this approach enhances external validity and could offer additional relevant insights that can be applied in clinical practice.

2. Treatment Effectiveness for Borderline Personality Disorder

Herein addressed several questions regarding the BPD treatment literature in a new way. To estimate treatment effects across BPD domains, herein included the pre- to post-treatment data from all treatments and outcome domains.

The effect sizes estimated at one year indicated that ST and reduced DBT showed the strongest changes in BPD outcome domains compared to the average treatment effect. Based on the outlier analyses, MBT was also related to larger effect sizes compared to the average. The untransformed sensitivity analyses indicated larger effect sizes of ST and MBT, and, less robustly, also of CBT. TAU and, to a lesser degree, CTBE were related to weaker improvements in all BPD outcome domains. The findings for CTBE were not as robust as those for TAU, which is not surprising as CTBE is generally viewed as an optimized variant of TAU ^[19]. The difference of TAU compared with the average effect was small, but medium compared to ST and reduced DBT. Together, these findings suggest that mainly the specialized treatments, i.e., ST, MBT and reduced DBT, appear to yield the largest effect sizes in the treatment of BPD compared to the average of all treatments. Overall, it should be emphasized that the average effectiveness of the treatments was moderate to large. With regard to the individual treatment effects, each treatment was compared to the average effect of all treatments. Thus, if some treatments were found to be related to larger effect sizes, this does not imply any specific differences between two individual treatments (as this is a different comparison that requires a more specific, more direct test).

Compared to the average, reduced DBT, and not DBT, was related to higher treatment effects. This is surprising, because it suggests that, compared to all treatments, a reduced version of DBT, and not the complete treatment model, is related to larger effect sizes, although the effect size difference between both treatments was small (g = 0.226). This is in accordance with one previous meta-analysis that showed that DBT yielded a moderate effect size compared to TAU, but a small effect size compared to specialized treatments $\begin{bmatrix} 1.7 \end{bmatrix}$. However, a few factors should be considered when interpreting this finding. First, the effective ingredients of reduced DBT have not yet been identified. Second, reduced DBT treatment models were very heterogeneous (i.e., studies omitted different DBT components), thereby possibly influencing these findings. Third, it is possible that some elements of DBT do not contribute to its effectiveness.

Herein also examined the changes in separate BPD domains. All domains showed moderate to large improvements, but the strongest improvement was observed for general BPD severity and affective instability. Impulsivity, suicidality/self-injury, anger and dissociation showed the least improvement compared to the average. Complex BPD symptoms such as suicidality/self-injury, impulsivity and intense anger have indeed been identified as relatively resistant to change $^{[20]}$. In contrast with our findings, one study showed that affective instability was relatively resistant to change during a two-year treatment $^{[21]}$. However, these findings cannot easily be compared to ours as it was unclear if and what type of treatment patients received in this study. Interestingly, a recent network study found that affective instability was not only central to the BPD criteria but was also central to the changes in these criteria $^{[22]}$. This means that affective instability is strongly related to other symptoms and that changes in affective instability are an important mechanism for change in other symptoms. This partly supports the finding that the strongest changes compared to the average were observed for this symptom. An alternative reason why some domains might show less improvement is that specific treatments may focus more strongly on some symptom domains than on others.

Exploration of the interaction between treatment and BPD criteria was largely consistent with the main findings. With large effect sizes, ST and MBT were robustly related to larger reductions in suicidality compared to the average treatment effect. Reduced DBT showed the largest improvements in anger and affective instability. In the untransformed sensitivity analysis, ST was related to the largest change for the criteria that showed the least improvement overall (i.e., impulsivity, suicidality, anger and dissociation), while DBT was associated with strong improvements in anger. Based on all analyses, with effect sizes ranging from small to large, TAU was related to smaller outcomes for seven BPD criteria, i.e., general severity, impulsivity, suicidality, emptiness, anger, affective instability and dissociation. These findings are in line with the general trends of our study, as the treatments with the highest (and lowest) effect sizes also had similar effect sizes on separate outcome domains. This is a very relevant issue for clinical practice, as more knowledge about these interactions can improve the development and effectiveness of personalized treatment in which patients are matched to treatments based on their symptom profiles. Thus, these findings raise interesting new leads for future studies, but more research is necessary to further test and examine these interactions.

The findings are consistent with earlier studies ^{[5][6]} and with the most recent meta-analysis in this area ^[Z]. In most cases, these previous studies have not found any differences between the specialized treatments and other protocolized treatments, but only with TAU. The effect sizes in the meta-analysis by Storebø et al., (2020) and the present one, representing differences between TAU and all other treatments in reducing general BPD severity (d = -0.52 vs. g = -0.74) and suicide-related outcomes (d = -0.34 vs. g = -0.25), were very similar. Moreover, where Storebø et al., (2020) found an effect size of d = -0.60 comparing DBT and TAU in reducing BPD severity, the present study found a difference of g = -0.76, and our findings also suggested that TAU was less effective compared to the joint other treatments in reducing general severity. Similarly, Storebø et al., (2020) also found that MBT, compared to TAU, was more effective in reducing suicidality. There were, however, differences in the number of studies that were available for each of these treatments. While many DBT trials were included, the number of ST, MBT and reduced DBT studies was smaller (between 9 and 11 studies). Therefore, it is possible that the meta-analytic findings of the specialized treatments with fewer studies were more prone to sources of bias. This is an important reason why it is important to also conduct more primary treatment studies focusing on these specialized models, as was also noted in previous meta-analyses, e.g., ^{[S][Z]}.

The models also identified several additional predictors of BPD treatment outcomes. Higher age was related to smaller improvements in BPD severity, consistent with the idea that personality becomes more resistant to change with increasing age $\frac{16|[23]}{2}$. Even though this effect appeared to be small, the difference in treatment effectiveness can become quite large when the difference in age increases. To illustrate, there is a medium difference in effect between a 20-year-old patient and a 40-year-old patient of 0.42. However, we should interpret this finding with caution as, within individual studies and treatment arms and due to Simpson's paradox $\frac{[24][25]}{12}$ in which aggregation of effects can lead to a reversal of effects, the opposite could also be true.

In addition, the largest improvement was found on outcomes describing the number of patients who still meet the DSM criteria for BPD after treatment, compared to outcomes based on continuous scores. Dichotomous outcomes (i.e., proportions) are measured on a different scale and are usually based on some cut-off score. Consequently, patients might still fulfill some criteria to a rather severe degree and suffer from BPD manifestations that do not qualify for a BPD diagnosis. Continuous outcome measures might therefore be less sensitive to this bias. A final interesting predictor was the way trials handled missing data. Completer analyses are generally not recommended because they use biased samples ^[26]. Therefore, the fact that we did not observe differences between completer analyses and modern ITT techniques was unexpected. Interestingly, for the untransformed effect sizes, LOFC, with a moderate effect size, was related to a smaller effect compared to other analysis types. This is in line with the often-heard suggestion that LOFC methods are very conservative and thus produce smaller effect sizes ^[27].

The findings also suggest that treatment format, setting, education level, assessment type, substance use exclusion, medication policy, country of testing and male proportion are not related to treatment outcomes. However, the proportion of males was generally very low and could also be indicative of a gender bias. The true proportion of male patients with BPD is likely higher ^[28] than in the meta-analyzed studies, which decreases the generalizability of our findings to male BPD patients. Moreover, as publication year was not related to treatment outcomes, there are no indications that, despite all developments, psychological treatments of BPD have improved over the years. Note, however, that the most effective specialized treatments were developed and tested rather recently (the mean publication years for MBT and ST were 2014 and 2012, respectively). In addition, earlier trials might have been conducted on a smaller-scale and might have been more susceptible to bias. Larger and more recent trials could have had a better methodological quality. Therefore, it is possible that while treatments improved, these effects were cancelled out by an improvement in overall study quality. However, we found no relationship between trial type and study quality, and the treatment outcomes, which corresponds to earlier findings ^[17], supporting our decision to include non-RTCs and uncontrolled studies. Also, we found indications

that longer BPD treatments were more effective, but this is inconsistent with earlier findings ^[5]. Lastly, our findings were relatively robust to outliers and appeared unaffected by publication bias ^[29].

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