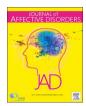
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#### Research paper

# The impact of personality disorder pathology on the effectiveness of Cognitive Therapy and Interpersonal Psychotherapy for Major Depressive Disorder



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#### ABSTRACT

*Background:* Despite extensive research, there is no consensus how Personality Disorders (PD) and PD features affect outcome for Major Depressive Disorder (MDD). The present study evaluated the effects of PD (features) on treatment continuation and effectiveness in Cognitive Therapy (CT) and Interpersonal Psychotherapy (IPT) for MDD.

*Methods*: Depressed outpatients were randomized to CT (n=72) and IPT (n=74). Primary outcome was depression severity measured repeatedly with the Beck Depression Inventory-II (BDI-II) at baseline, three months, at the start of each therapy session, at post-treatment and monthly during five months follow-up.

Results: Comorbid PD and PD features did not affect dropout. Multilevel and Cox regression models indicated no negative effect of PD on BDI-II change and remission rates during treatment and follow-up, irrespective of the treatment received. For both therapies, higher dependent PD features predicted overall lower BDI-II scores during treatment, however this effect did not sustain through follow-up. Cluster A PD features moderated treatment outcome during treatment and follow-up: individuals with high cluster A PD features had greater BDI-II reductions over time in CT as compared to IPT.

*Limitations*: Not all therapists and participants were blind to the assessment of PD (features), and assessments were performed by one rater. Further research must investigate the state and trait dependent changes of PD and MDD over time.

Conclusions: We found no negative impact of PD on the effectiveness and treatment retention of CT and IPT for MDD during treatment and follow-up. If replicated, cluster A PD features can be used to optimize treatment selection.

#### 1. Introduction

Individuals with major depressive disorder (MDD) often meet criteria for DSM defined co-morbid personality disorders (PD), in particular PD's grouped in cluster C: obsessive compulsive PD, dependent PD and avoidant PD (Friborg et al., 2014). Despite extensive research spanning several decades, results from research into the impact of comorbid PD on the effectiveness of acute phase treatment for MDD is equivocal; results vary from a negative association between the presence of a co-morbid PD and clinical outcome (Hardy et al., 1995;

Newton-Howes et al., 2014; Reich and Vasile, 1993; Sato et al., 1994) to the absence of any difference between outcome in individuals with and without co-morbid PD (De Bolle et al., 2011; Kool et al., 2005; Moradveisi et al., 2013; Mulder, 2002). These inconsistencies across studies are probably best explained by methodological problems. Uncontrolled study designs are common, allowing selection bias based on clinicians' decision-making. Nevertheless, the studies that used a randomized design also reported inconsistent findings varying from no differences between individuals with and without a co-morbid PD (Hirschfeld et al., 1998; Maddux et al., 2009) to a negative effect of PD

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on MDD outcome (DeRubeis et al., 2014; Fournier et al., 2008). Another concern is that only a few studies provide data on the relationship between PD and dropout (Kool et al., 2005), which can lead to biased or inaccurate conclusions. The few studies that reported drop-out rates have mixed results: some showed no difference between individuals with and without PD (Fournier et al., 2008; Kool et al., 2003; Sullivan et al., 1994), while others reported higher drop-out rates for individuals with PD (Moradveisi et al., 2013). In addition, despite substantial differences (e.g. depression severity) between individuals with and without PD, multivariable models controlling for significant confounders are rarely used (Casey et al., 2004; Mulder, 2002). Finally, inconsistent findings could also be explained by different outcomes on self-report versus clinician-rated measures of personality pathology and depression outcome (Mulder, 2002; Stanley and Wilson, 2006; Unger et al., 2013).

Concerning the various treatment options for MDD, researchers and clinicians alike have come to realize that a 'one size fits all' approach is not very effective. A major challenge in health care research today is to select the best treatment option for a given individual, a concept referred to as *personalized medicine* (Simon and Perlis, 2010). Therefore, it is highly relevant to examine whether depressed individuals with comorbid PD respond differentially to evidence-based psychotherapies for MDD. At present, both Cognitive Therapy (CT) and Interpersonal Psychotherapy (IPT) are recommended as first choice evidence-based psychotherapies for MDD (Cuijpers et al., 2014). A recent trial sequential analysis showed that both treatments do not differ in effectiveness for MDD when a difference of 4 BDI-II points is taken as futile (Lemmens et al., 2015).

Previous research comparing CT and IPT head-to-head suggests specific PD features as potential treatment moderators. The National Institute of Mental Health Treatment of Depression Collaborative Program found that depressed individuals with obsessive-compulsive PD features were more likely to respond to IPT, while depressed participants with more avoidant PD features responded better to CT (Barber and Muenz, 1996). These results were partially replicated by the Christchurch Psychotherapy for Depression Study, where individuals with MDD and comorbid PD features responded less well to IPT compared to CT (Carter et al., 2011) particularly in individuals with avoidant PD features (Joyce et al., 2007). In another study, depressive PD features predicted better outcome in CT compared to IPT, while other PD features did not predict differential treatment outcome (Ryder et al., 2010). These inconsistencies might be explained by the use of different PD assessments, which complicates comparison of these findings. Moreover, most studies use simple linear regression models, while multilevel modeling is rarely used. The latter can explore the dynamic and individual course of depression more accurately (De Bolle

The overall aim of the current study was to determine whether the presence of a DSM PD diagnosis, affected depressive symptom change and treatment retention in CT and IPT during treatment and follow-up. In addition, the effect of PD on remission rates was evaluated, since achieving remission is an evident treatment goal in CT and IPT. Potential differences in these effects between CT and IPT were examined. To acquire a more detailed understanding about cluster C PD features, dimensional scores of obsessive-compulsive, avoidant and dependent PD features as defined by the DSM were calculated, together with cluster A and cluster B PD feature scores. With these scores, general and differential effects of specific PD features on depressive symptom change, treatment retention and remission were examined in CT and IPT. Based on previous studies, we were unsure how PD affected depression outcomes and dropout in CT and IPT during treatment and follow-up. Based on the previous comparisons between CT and IPT we expected cluster C features, in particular obsessive-compulsive and avoidant PD features to moderate treatment outcomes.

#### 2. Methods

#### 2.1. Design and participants

Data were collected in the context of a large randomized clinical trial. A detailed description about sample characteristics, study design, interventions, and main treatment outcome findings is provided elsewhere (Lemmens et al., 2011; Lemmens et al., 2015). The study was conducted at the mood disorders unit of the Maastricht Community Mental Health Centre (RIAGG Maastricht) and included 182 outpatients, 18–65 years of age, with a primary diagnosis of MDD (as confirmed with the Structured Clinical Interview for DSM-IV Axis I disorders (SCID-I; First et al., 1995)). Other inclusion criteria were: internet access, an email address, and sufficient knowledge of the Dutch language. Exclusion criteria were a bipolar or chronic (current episode > 5 years) depression, high acute suicide risk, concomitant pharmacological or psychological treatment, drugs and alcohol abuse/dependence, and mental retardation (IQ < 80).

Participants were randomly allocated to CT (n=76), IPT (n=75), or a Waiting List Condition (WLC; n=31). For the current analyses, we limited the sample to data of individuals randomized to CT and IPT (n=151). This sample participated in a treatment phase (0-7 months) and a subsequent trial follow-up phase (7-12 months). Five participants (4 in the CT group and 1 in the IPT group) were excluded in the current study, because PD assessments were incomplete or missing. All participants provided written informed consent and the study was approved by the Medical Ethics Committee of Maastricht University Medical Center. The study is registered at The Netherlands Trial Register, part of the Dutch Cochrane Centre (ISRCTN 67561918).

#### 2.2. Measures

#### 2.2.1. Primary outcome

Primary outcome, depressive symptom severity, was assessed with the Beck Depression Inventory, second edition (BDI-II; Beck et al., 1996). BDI-II measurements included in this study were collected at baseline, at the start of each therapy session and at 3, 7, 8, 9, 10, 11, and 12 months.

#### 2.2.2. Personality measures

PD diagnoses were administered prior to treatment using the Structured Clinical Interview for DSM-IV Axis II (SCID-II; First et al., 1997) by well-trained therapists that were participating in the study. In addition, the results of the SCID-II assessment were available in the patient record during treatment. Therefore, therapists and participants were not blind to the results of the SCID-II assessment. Passive-Aggressive PD and Depressive PD were excluded from the analyses, given their position in the section of criteria sets for further study (American Psychiatric Association, 2000). Dimensional PD scores were calculated by summing up the items answered with 'present' for each PD criterion, dismissing items that were scored 'uncertain' or 'absent'. For the cluster C PD features, we calculated individual avoidant PD features scores (range 0-7), dependent PD features scores (range 0-8), and obsessivecompulsive PD features scores (range 0-8). We calculated individual cluster A PD features (range 0-23) and cluster B PD features (range 0-41) total scores providing two reference groups of other, non-Cluster C, PD features.

#### 2.3. Treatments and therapists

Both interventions consisted of 16–20 sessions of 45 min, depending on the participants' improvement, with an average of 17 sessions per person (SD = 2.9; Lemmens et al., 2015). Sessions were planned weekly and allowed to be less frequently scheduled towards the end of therapy.

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