

**Personality and Outcome in Individuals with Treatment-Resistant Depression -
Exploring Differential Treatment Effects in the Tavistock Adult Depression
Study (TADS)**

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Abstract

Objective: Although research over the past decades has investigated the impact of the personality dimensions of dependency and self-criticism on treatment outcome, little is known of how these personality features influence responsiveness to treatment in patients with severe, chronic forms of depression. **Method:** The present study uses data from the Tavistock Adult Depression Study (TADS), a randomized controlled trial investigating the effectiveness of long-term psychoanalytic psychotherapy (LTPP) compared with treatment as usual (TAU) for individuals diagnosed with treatment-resistant depression. Patients were rated with the Anaclitic Introjective Depression Assessment Q-sort, which distinguishes between two more maladaptive (*Submissive* and *Dismissive*) and two less maladaptive (*Needy* and *Self-Critical*) subdimensions of dependent or anaclitic and self-critical or introjective depression. Multilevel modeling was used to compare individuals' growth curves of depression severity as measured by the Hamilton Rating Scale for Depression over the 18-months treatment period and two-year follow-up. Rates of clinically significant change were also determined. **Results:** As expected, depressed patients with more maladaptive dependent and self-critical features did not benefit from LTPP or TAU. Patients with less maladaptive self-critical features benefitted from both LTPP and TAU, while those with less maladaptive dependent features showed considerable gains from LTPP but not from TAU, with medium to large effect sizes. **Conclusions:** Findings of this study are consistent with existing research suggesting the need to modify and tailor treatments in accordance to individuals' pre-treatment personality features. Given the time and cost-intensive nature of longer-term treatment, this may be particularly important in patients with treatment-resistant depression.

Keywords: anaclitic; introjective; AIDA; treatment-resistant depression; differential treatment effects

Public Health Significance Statement

Patients with treatment-resistant depression characterized by a preoccupation with relatedness and self-definition at different developmental levels showed differential trajectories of change in both long-term psychoanalytic psychotherapy and treatment as usual. Existing treatments for treatment-resistant depression may need to be modified for patients with more problematic and maladaptive personality features. Therapists should adapt their therapeutic techniques to underlying personality features in order to achieve better treatment outcomes.

There has been a long tradition of studies investigating the impact of personality on treatment outcome in depression and other mental health conditions (e.g., Blatt, 1992; Blatt & Ford, 1994; Blatt & Shahar, 2004; Fertuck, Bucci, Blatt, & Ford, 2004; Joyce, Ennis, O'Kelly, Ogrodniczuk, & Piper, 2009; Vermote et al., 2009; Vermote et al., 2011; Werbart & Forsström, 2014). However, very few studies have focused on patients with more complex and protracted forms of depression. As a consequence, these individuals are currently at a serious disadvantage in terms of their clinical management (Town, Abbass, Stride, & Bernier, 2017). Much of the available research concerning the influence of personality on treatment response in depression has originated from the two-configurations model developed by Blatt and colleagues (1974, 2004). This model distinguishes between two personality dimensions in depression. Issues in *anaclitic depression* are centered on dependency and need gratification, and are predominantly expressed in feelings of emptiness and loneliness, and intense fears of being abandoned and left unprotected. Issues of self-definition, which include an overemphasis on feelings of worthlessness, guilt, blame, and extreme self-criticalness, are, on the other hand, hypothesized to be typical of *introjective depression*. Embedded within the model is the assumption that these two personality organizations are hierarchically organized. As such, anaclitic or introjective patients may express their dependent or self-definitional problems at different development levels, ranging from basic or more maladaptive to higher and more adaptive levels of respective struggles (Blatt, 1995; Blatt, Zuroff, Hawley, & Auerbach, 2010). Anaclitic and introjective depressed patients would not only bring different key issues, topics, and themes to therapy; they would also respond in different ways to the unfolding therapeutic process (Blatt & Felsen, 2010; Blatt et al., 2010). While anaclitic patients may constantly seek the therapist's reassurance, and experience difficulties with the inevitable ruptures in the therapeutic relationship (e.g. around holidays), introjective patients are assumed to become involved in struggles around issues of power and autonomy, and may

increasingly become competitive and critical of the therapist's interventions. As such, for any therapy to be effective, its techniques would have to be adapted to these particular underlying personality features and their different concerns and needs (e.g., Blatt, 2004; Blatt & Auerbach, 2001; Blatt et al., 2010; Bleichmar, 2010; Fonagy, Luyten, & Bateman, 2015; Werbart & Levander, 2016). Existing research has indeed shown that both personality dimensions may influence treatment outcome, regardless of treatment modality. This has been shown for Psychodynamic Therapy, Interpersonal Therapy (IPT), and Cognitive-Behavioral Therapy (CBT) (Blatt et al., 2010; Shahar, Blatt, Zuroff, & Pilkonis, 2003). Furthermore, failure to adapt treatment to patients' features has been shown to be related to worse therapeutic outcomes (e.g., Watzke et al., 2010).

Patients who struggle with self-definitional issues (i.e. introjective patients) typically show poor outcomes in brief treatments for depression. Studies in this area suggest that the arbitrary time limit of such brief treatments would interfere with these individuals' need for control and mastery, and would also impair the formation of a working alliance (Shahar et al., 2003). By contrast, these patients have been found to respond significantly better to more insight-oriented, longer-term psychoanalytic treatments than to brief therapies, such as CBT, Supportive-Expressive Psychotherapy (SEP), or IPT (Blatt et al., 2010). An insight-oriented approach would match these patients' particular cognitive-affective style (Blatt & Ford, 1994; Fonagy et al., 1996), and considerable time would be needed for them to establish a safe working alliance, which in turn would facilitate the therapeutic work (Blatt, 2004).

Evidence for the role of dependency issues in depression and its treatment has been somewhat less strong (Shahar, 2015). However, several longitudinal studies have shown that dependency, and particularly maladaptive expressions of dependent features, as captured by the neediness subscale of the Depressive Experience Questionnaire (DEQ, Blatt, D'Afflitti, &

Quinlan, 1976), confer risk for depression (e.g. Mongrain & Leather, 2006; Schulte, Mongrain, & Flora, 2008). Furthermore, patients who struggle with interpersonal issues (i.e. anaclitic patients) have been found to benefit less from insight-oriented treatments and more from SEP, as the former type of treatment may be inconsistent with their need for support and validation (Blatt & Shahar, 2004; Fertuck et al., 2004). Very few studies are available that have focused on so-called mixed dependent and self-critical patients. Shahar, Blatt, and Ford (2003), for instance, found these individuals to be clinically more impaired than dependent and self-critical patients. Yet, interestingly, patients in this mixed group showed greater improvements in psychoanalytic oriented treatment compared to dependent and self-critical patients. Clearly, more research is needed in this area, in particular as differential treatment effects might also be expected to emerge when patients who are struggling with issues of relatedness and self-definition at different developmental levels are compared.

A recently developed observer-rated measure, the Anaclitic-Introjective Depression Assessment (AIDA; Rost, Luyten, & Fonagy, 2017), identified four naturally occurring clusters of patients diagnosed with treatment-resistant depression based on Blatt's theoretical formulations. Consistent with Blatt's assumptions, individuals in all four clusters did not differ in terms of depression severity, but showed large differences in terms of intrapersonal and interpersonal functioning. Two clusters, termed *Needy Depression* and *Self-Critical Depression*, were characterized by lower levels of psychopathology and fewer problems in terms of occupational, social, and relational functioning. The other two clusters, termed *Submissive Depression* and *Dismissive Depression*, described patients with more severe issues related to dependency and self-definition, expressed in significantly higher levels of psychopathology and lower levels of interpersonal and occupational functioning. In contrast to the clinical presentation of mixed patients in Shahar et al., (2003), the Heterogeneous group did not distinguish from the other AIDA clusters in terms of depression severity or

clinical presentation. Overall, they presented on a similar functioning level to the two more maladaptive clusters.

In this context, it is important to note that there is now consensus that the more problematic or pathological the personality organization is, the more modifications of the treatment approach might be required in order to achieve a good outcome (Clarkin, Levy, Lenzenweger, & Kernberg, 2007; Fonagy & Bateman, 2006; Piper, Joyce, McCallum, Azim, & Ogrodniczuk, 2002). Consistent with this assumption, a systematic review of studies investigating the relationship between levels of personality organization and treatment outcome found that patients with more adaptive levels showed a better response to psychotherapy at the end of treatment and after 3–5-year follow-up compared with patients with lower levels (Koelen et al., 2012).

The Present Study

The present study uses data from the Tavistock Adult Depression Study (TADS; Fonagy, Rost, et al., 2015). The TADS is a randomized controlled trial that compared once-weekly long-term psychoanalytic psychotherapy (LTPP) versus treatment as usual (TAU) in a sample of 129 patients diagnosed with treatment-resistant depression. TAU consisted of a wide range of short-term therapies recommended by the National Institute for Health and Clinical Excellence (NICE; 2009), including Cognitive Behavioral Therapy (CBT), Counseling, and other brief psychotherapies. At the 24-month follow-up, 30% of those who received LTPP were in partial remission compared with only 4% who received TAU. Given the chronicity and substantial comorbidity of this sample, these results are promising; however, they also indicate that a substantial proportion of patients did not show sustained benefits. The aim of the present study was to shed further light on to these findings by investigating the potential impact of levels of anaclitic and introjective personality features on treatment outcome.

In line with theoretical assumptions and empirical findings reviewed above, we expected patients with less maladaptive anaclitic or introjective personality features (*Needy Depression* and *Self-Critical Depression*) to show greater benefits receiving treatment, while depression scores for those with more maladaptive anaclitic or introjective personality features (*Submissive Depression* and *Dismissive Depression*) were expected to change less as a function of receiving treatment. Patients who fell into two or more of these clusters were grouped together (the *Heterogeneous Group*), and were expected to benefit less from treatment given their complex presentation.

Method

Participants

The study included 39 male and 81 female patients with a diagnosis of current major depressive disorder (MDD) and at least two failed previous treatment attempts. Ninety-seven patients (81%) had an additional diagnosis of early-onset dysthymia. The average lifetime duration of depression was 25.4 years ($SD = 12.42$) and the average length of the current MDD episode was 3.7 years ($SD = 3.0$). The majority of patients (81%) were white Caucasian and they ranged in age from 22 to 66 years ($M = 44.0$, $SD = 10.31$). The study was approved by the Institutional Review Board of NHS West Midlands Research Ethics Committee (MREC02/07/035) and patients provided informed written consent prior to randomization.

Assessments and Measures

Participants received extensive research and clinical diagnostic assessments at baseline before randomization. Primary and secondary outcome measures were collected at 6-monthly intervals during the 18-month treatment period and then at 24, 30, and 42 months follow-up.

Depression Severity. In line with the primary outcome measure of the TADS, treatment outcome was defined in terms of scores on the Hamilton Rating Scale for Depression (HRSD; Hamilton, 1967). The HRSD is the most widely used interview-based measure of severity of depression, with acceptable psychometric properties (Nezu, Ronan, Meadows, & McClure, 2000). It consists of 17 items, which yield a range of scores from 0–53 with the following severity indicators: 0–7 not depressed, 8–13 mild depression, 14–18 moderate depression, 19–22 severe depression, >23 very severe depression. All ratings were carried out by two independent blinded assessors. Inter-rater reliability was excellent with an Intraclass Correlation Coefficient of 0.89.

Levels of Personality Features. The Anaclitic and Introjective Depression Assessment (AIDA; Rost et al., 2017) was utilized to assess the levels of interpersonal dependency and self-definition of each of the TADS participants. The AIDA is an observer-rated Q-sort measure that was developed using Q-sort methodology (Block, 1961; Stephenson, 1953) and expert consensus rating. It consists of 59 personality-descriptive statements, derived from the item pool of the well-established Shedler-Westen Assessment Procedure (SWAP-II; Shedler & Westen, 2007). Example items for dependent personality are “*Tends to fear he/she will be rejected or abandoned*” and “*Tends to be insufficiently concerned with meeting own needs; appears not to feel entitled to get or ask for things he/she deserved*”. Example items for self-critical personality are: “*Appears to have little need for human contact; is emotionally detached or indifferent*” and “*Tends to feel he/she is inadequate, inferior, or a failure*”. Q-methodology follows a person-centered approach and entails the rank-ordering of each statement as per their relevance or prototypicality in describing an individual using a pre-determined rating scale and fixed distribution to categorize these. The personality statements are furthermore required to be rank-ordered relative to each other in order to obtain a *composite description* or *gestalt* of a prototypical

personality (Westen & Shedler, 1999). Inverse factor analysis (also known as Q-factor analysis) can subsequently be carried out to identify latent clusters of personality prototypes. For the AIDA, each statement is rank-ordered on a 5-point rating scale following a fixed distribution: 20 items are to be sorted into category 1 (not at all prototypical), 14 items into category 2 (slightly prototypical), 11 items into category 3 (somewhat prototypical), 8 items into category 4 (next most prototypical), and 6 items into category 5 (most prototypical). The shape and range of the AIDA mirrored that of the SWAP-II as it also aimed at identifying the most prototypical personality features only and in order to control for rater effect and minimization of error variance, it utilized a fixed distribution (Block, 2008).

Carrying out an inverted Principal Component analysis with Promax rotation, Rost et al. (2017) identified four clusters of depressed patients explaining 46.5% of the total variance: two subdimensions of the anaclitic configuration, named *Submissive Depression* and *Needy Depression*; and two subdimensions of the introjective configuration, named *Dismissive Depression* and *Self-Critical Depression*. Figure 1 provides a summary description of these clusters. Cronbach's alpha for all factors were $\geq .8$ suggesting adequate internal consistency (Fleiss, 1981). Examination of the items' content revealed that issues with dependency of the *Needy Depressed* are expressed and managed at a more intermediate level compared to those of the *Submissive Depressed*. For example, whilst the former seek attention and care out of fear to be rejected or abandoned, the latter are driven by a belief that the self is bad, damaged and unworthy of love and care, often leading to abusive relationships. Similarly, *Self-critical* and *Dismissive Depressed* both express exaggerated concerns of self-definition, however, the distinguishing factor appears their ability to relate to others and their view of themselves expressed at different developmental levels. *Dismissive Depressed* are governed by intense denial of the need for relatedness, which manifests in extreme dismissiveness and criticalness of others whilst the self is seen as superior or

idealized. *Self-critical Depressed* are more fearful avoidant, they function moderately well but still struggle to internalize their success and thereby reduce their harsh self-criticalness. Evidence for convergent and discriminant validity was supported, showing expected relationships with expert anaclitic and introjective prototypes and various functioning indices, including clinical, social, occupational, global, and interpersonal functioning (Rost et al., 2017), and with interpersonal problems (Miller & Hilsenroth, 2017). In summary, *Needy Depression* and *Self-Critical Depression* were associated with lower levels of psychopathology and fewer problems in terms of occupational, social, and relational functioning. These patients were more likely to have a university degree, be in employment, have some meaningful interpersonal relationships, and report fewer episode of self-harm, suicidality, and substance abuse. *Submissive Depression* and *Dismissive Depression* were associated with significantly higher levels of psychopathology and lower levels of interpersonal and occupational functioning. The majority of these individuals had no formal education and they were mainly unemployed. They reported higher rates of self-harm, suicidality, and substance abuse. While the *Dismissive Depressed* patients avoided relationships, the *Submissive Depressed* individuals showed a tendency to have abusive partners.

The AIDA was rated for all TADS participants by the first author, and 51 patients (41%) were double-rated by an independent researcher. Both raters familiarized themselves with the manual (available from the authors) and were trained in Q-sort methodology. The ratings were done retrospectively after listening to extensive research and clinical material collected at study intake (for more detail, see Rost et al., 2017). Both raters were blind to the participants' group allocation and independent from the assessment of depression severity. Inter-rater reliability was assessed using the Intraclass correlation coefficients (ICCs). ICCs were calculated using the two-way random effects model with Spearman–Brown correction,

presenting the mean reliability across two raters (Shrout & Fleiss, 1979). Mean single-rater ICC was .86 (range = .32–1) and the ICC across both raters was .86 (range: .69–.95), providing good to excellent inter-rater reliability (Fleiss, 1981). In the present study, categorical allocations were made by assigning patients to the AIDA cluster for which they received the highest Q-score, provided that the correlation was ≥ 0.40 and the loading was at least 0.10 higher than on other factors (Bradley, Heim, & Westen, 2005). Overall, 120 of the 129 (93%) TADS participants were categorized, with 30 falling within Self-Critical Depression, 16 within Dismissive Depression, 29 within Submissive Depression, and 18 within Needy Depression. Twenty-seven patients had positive correlations on more than one factor and were categorized as the “Heterogeneous Group”. Eight patients could not be categorized and were thus removed from the analysis.

Treatment and Control Conditions

A detailed description of the TADS design is available elsewhere (Taylor et al., 2012). In summary, patients were randomized to LTPP or TAU. LTPP consisted of 60 once-weekly psychoanalytic psychotherapy over 18 months (mean number of sessions attended was 41). LTPP was carried out by 22 senior psychotherapists (mean years of experience was 17.45 years) from the adult department of the Tavistock Clinic, UK. The treatment approach is manualized (Taylor, 2015) and focuses in particular on a time-limited psychoanalytic treatment framework specified for treatment-resistant depression. The treatment model is not influenced by Blatt’s conceptualization of the two fundamental configurations of depression, and can primarily be described as object-relational with Kleinian and post-Kleinian influences. It is primarily aimed at helping the patient uncover and explore recurrent patterns of behaviors, emotions, and relationships and to link present experiences with past events and early development. The therapist’s observations and understanding are verbalized in the form of interpretations, with a particular emphasis on the emerging relational patterns between the

patient and the therapist in the here-and-now (transference interpretations). TAU consisted of a wide range of short-term psychotherapeutic interventions as recommended by UK national treatment guidelines (NICE, 2009). Overall, 44% of patients randomized into this group received at least one treatment, including CBT (13%), counseling (24%), and other types of psychotherapy (7%). The mean number of attended therapy sessions in TAU was 10.

Eighty percent of patients in both treatment groups were on prescribed antidepressant medication during the treatment phase, which reduced slightly to 70% over the course of follow-up. Eleven percent of those randomized to LTPP also received additional psychotherapy. During the follow-up period, 38% of patients in both treatment groups were referred to at least one short-term treatment. Table 1 provides a breakdown of treatment allocation and additional treatment received for all AIDA clusters. In terms of additional treatments received, no statistical significant differences between the clusters were found.

Analysis Design

HRSD scores were normally distributed at baseline; thus, parametric statistics were used. As the data followed a hierarchically nested structure on two levels, repeated-measures time points (level 1) nested within patients (level 2), it was analysed by fitting growth curve models, also known as multilevel modelling (Rabe-Hesketh & Skrondal, 2012). This allowed the simultaneous estimation of how depression scores change over time and how particular covariates affect the trajectory of change. As the present study is an extension of the TADS analysis, the final model in that original report was utilized as the starting point (Fonagy et al., 2015). This included a linear and quadratic time variable, university degree as a covariate to control for significant baseline differences between treatment groups, and a random slope for the linear time term. As differences with regard to educational status were also statistically significant between AIDA clusters (see Appendix S1), we retained this variable as a covariate.

In order to test whether the differential linear trajectories of change linked to treatment varied across the AIDA clusters, as hypothesized, we added the AIDA cluster and their two-way interactions (linear time \times AIDA cluster and group \times AIDA cluster) and three-way interactions (linear time \times group \times AIDA cluster) as covariates into the model. Because the data included missing data, we used multiple imputation (MI) to estimate model parameters and their standard errors (details provided below). For MI data, the general rule for assessing the goodness of fit by carrying out the likelihood ratio test could be applied. Therefore, the fit of nested models was compared by testing whether the relevant multiple coefficients were jointly significantly different from zero (Rubin, 1987). Initial analyses showed that the random slopes of linear time were statistically non-significant and therefore this random term was removed from the model.

Following the previous paper from this study (Fonagy et al., 2015), seven time points were coded as -7 (baseline), -6 (6 months), -5 (12 months), and -4 (18 months) of the treatment period, and -3 (24 months), -2 (30 months), and 0 (42 months) of the follow-up. The regression coefficients involving time thus measured the linear rate of change from baseline to 42 month follow-up, and the intercepts referenced group differences at the 42 months follow-up point. Educational status was dummy coded as 0 (no university education) and 1 (university education), and the five AIDA clusters were dummy coded with Self-Critical Depression serving as the reference group (0), and treatment group allocation coded as 1 (LTPP) and 0 (TAU). To provide individual comparisons between all AIDA clusters in their treatment effects or treatment \times time interactions, we repeated the analyses five times, changing in each case which AIDA cluster was the reference group.

Data Imputation. Twenty-four percent of HRSD values were missing, which exceeds acceptance criteria and could jeopardize the robustness and validity of the statistical analyses carried out if not mitigated (Schafer, 1999). An MI technique was thus applied,

which can be considered the most robust method currently available for handling missing data (Donders, van der Heijden, Stijnen, & Moons, 2006). Following recommendations by Graham, Olchowski, and Gilreath (2007), 40 MI datasets were created, and subsequent analyses were carried out on the aggregated estimate using Rubin's (1987) rule.

Clinically Significant Change. In order to investigate the extent to which observed effects translated into clinically meaningful change, clinically significant change (CSC) was calculated in accordance with the Reliable Change Index (RCI; Jacobson & Truax, 1991). Reliable change was achieved when the RCI was ± 1.96 ($p < .05$). To have achieved CSC, the patient had to both reach reliable positive change and move out of the clinical distribution into the functional distribution. Number needed to treat (NNT) was calculated as the relevant effect size. All analyses were carried out using the STATA ME package utilizing the MI estimate command (StataCorp, 2013).

Results

Descriptive Characteristics and Preliminary Analyses

Apart from educational status, the five AIDA prototypes did not show any statistically significant differences in terms of demographic variables or baseline depression severity (see Appendix S1). As this study had a reduced sample size of 120 compared to the original TADS report (and the analyses were based on multiple imputations), prior to testing our hypotheses we checked whether the findings from the original TADS report (Fonagy et al., 2015) were similar in the current dataset. Participants in both LTPP and TAU showed significant reductions in mean depression severity over time; however, differences between the two treatment groups became statistically significant during the follow-up, with LTPP being associated with significantly smaller depression scores than TAU ($\beta = -.36$, $SE = .15$, 95% CI = $[-.66, -.07]$, $t = -2.39$, $p = .017$) (see Appendix S2).

Change trajectories of the AIDA prototypes

In order to test the current hypotheses, the analysis focused on whether the rate of change between the AIDA clusters differed as a function of treatment group (LTPP versus TAU). The model estimated trajectories of depression scores by treatment group, AIDA cluster and time as shown in Figure 2. The parameter estimates of the final growth model, shown separately with each AIDA cluster as reference group, are presented in Table 2. The AIDA cluster intercepts, which correspond to the mean depression scores at 42 month follow-up, showed that the Self-Critical Depressed group had lower mean depression scores compared with all other AIDA clusters with a difference of 4–6 points on the HRSD. These mean scores differed significantly from all the others. No other group differences in overall mean at follow-up were significant. The treatment effects at follow-up were generally largest for the Needy Depressed group ($\beta = -5.76$, $SE = 2.26$, 95% CI: [-10.19, -1.32], $t = -2.55$, $p = .0011$) and the Heterogeneous Group ($\beta = -3.59$, $SE = 1.74$, 95% CI: [-6.99, -0.18], $t = -2.07$, $p = .039$) and indeed only significant for these two groups. The treatment x AIDA cluster interactions showed that the effect of treatment was larger for the Needy Depressed group compared to the Self-Critical Depressed and Submissive Depressed groups, but no other differences in treatment effect were significant.

Considering changes over time, in general there was a consistent linear effect of time, with all groups showing declines in depressive symptoms and also a quadratic effect of time, indicating that rates of change slowed over time in all groups. AIDA clusters showed no statistically significant differences in linear rates of change overall, with the exception that the rate of improvement was weaker (i.e., less negative) in the Heterogeneous group compared to the Self-Critical Depression group ($\beta = 0.95$, $SE = 0.28$, 95% CI: [0.39, 1.5], $t =$

3.35, $p = .001$) and the Submissive Depression group ($\beta = -0.57$, $SE = 0.26$, 95% CI: [0.39, 1.50], $t = 3.35$, $p = .001$).

Consistent with the effects seen at follow-up, linear rates of improvement over time varied by treatment group only in the Needy Depression group and Heterogeneous groups (Needy: $\beta = -0.93$, $SE = 0.35$, 95% CI: [-1.62, -0.25], $t = -2.67$, $p = .008$; Heterogeneous: $\beta = -0.55$, $SE = 0.27$, 95% CI: [-1.08, -0.03], $t = -2.06$, $p = .040$). When the magnitude of difference in treatment-related change was compared between the AIDA clusters, the only significant difference was between the Needy Depressed group and the Self-Critical Depressed group ($\beta = -0.91$, $SE = 0.44$, 95% CI: [-1.76, -0.05], $t = -2.08$, $p = .038$). As can be seen in Figure 2, the change in depression scores was quite large in LTPP compared to TAU in the Needy Depressed group, a difference that was much less marked in the Self-critical Depressed group.

In a final step, we examined how these findings translated into CSC. Table 3 displays the observed pooled HRSD scores for each AIDA cluster, the corresponding severity index, and proportion of CSC. As hypothesized, both the Submissive and Dismissive Depression patients did not show any clinical significant change at the end of the follow-up. Noteworthy, however, is that 12 months into treatment, 44% of individuals with Dismissive Depression who received LTPP reached CSC, compared with 17% in TAU (RR = 0.56; 95% CI: [0.47, 0.67]; NNT = 2.3). For individuals with Submissive Depression at this time point, on the other hand, 24% of those in TAU reached CSC, compared with none in LTPP (RR = 1.31; 95% CI: [1.18, 1.57]; NNT = 4.2). However, any notable benefits gained were not retained by either AIDA cluster. Consistent with the MLM, individuals with Needy Depression who received LTPP showed increasing proportions of CSC at each follow-up point, with a notable peak at 30 months when 67% reached CSC (RR = 0.33; 95% CI: [0.25, 0.44]; NNT = 1.5). A notable relapse, however, can be observed at the last follow-up, when only 25% reached

levels of CSC (RR = 0.75; 95% CI: [0.67, 0.84]; NNT = 4). Individuals with Self-Critical Depression showed a very similar trajectory of change in both LTPP and TAU, showing an overall improvement in depression severity over time. However, at this time point, 33% of individuals with Self-Critical Depression who had received LTPP reached CSC, compared with only 17% of those in TAU (RR = 0.84; 95% CI: [0.73, 0.98]; NNT = 7.7). Apart from one individual who received LTPP, none of the individuals falling into the Heterogeneous group achieved CSC.

Discussion

The aim of the present study was to investigate whether pre-treatment personality features underlying treatment-resistant depression were differentially related to once-weekly LTPP compared with TAU. As hypothesized, the findings indicate clear differential outcome trajectories for the two less maladaptive (Needy and Self-Critical Depression) and the two more maladaptive (Submissive and Dismissive Depression) clusters, with patients in the latter clusters showing no sustained improvements in depression severity in LTPP or TAU. By contrast, both Needy Depressed and Self-Critical Depressed patients clearly benefited from treatment, and LTPP in particular.

In line with previous research, statistically significant main effects of personality were found in the present study, with both higher functioning introjective (Self-Critical) and anaclitic (Needy) and depressed patients benefitting from LTPP, and patients with Self-Critical Depression also benefitting from TAU. However, the present results also extend previous findings (Blatt & Auerbach, 2003; Blatt & Ford, 1994; Blatt & Shahar, 2004) by identifying a subgroup of anaclitically depressed patients who benefited significantly from LTPP, an insight-oriented and interpretative treatment. Indeed, previous studies found that individuals with issues focused around dependency did not respond well to LTPP (Blatt, 1992; Blatt & Shahar, 2004). Yet, these studies typically did not differentiate between

different levels of anaclitic patients. The present study found that higher functioning and less maladaptive Needy Depressed patients showed substantial improvements in depression severity, with large effect sizes in LTPP. At the 30-months follow-up, 67% of these patients in LTPP reached CSC. However, two-third of these patients relapsed into the moderate severity range a year later. One possible explanation might be that the end of treatment may have led to a reactivation of anaclitic issues that had not been worked through sufficiently. This may also explain why 33% of these patients sought additional treatment during the follow-up. It could also be that dependency issues might be more difficult to change, which in turn would provide further evidence for the role of anaclitic issues in depression. Further research is needed here, and a follow-up study will explore the therapeutic process in these patients using the Psychotherapy Process Q-Set (Jones & Ablon, 2005).

Patients with Self-Critical Depression showed a very different trajectory of change, in that the average growth curve was not as steep and severity of depression decreased much more gradually over time compared with those with Needy Depression. Fewer patients reached CSC overall; however, of interest is the reverse pattern of change observed at the last follow-up compared to Needy Depressed patients. The percentage of those with Self-Critical Depression reaching CSC increased by two-third from 30-months to 42-months follow-up. Moreover, although these individuals also benefited from TAU, at the last measurement point, they benefitted more from LTPP, with those receiving the psychoanalytic treatment being almost three times more likely to reach CSC as those in TAU. These findings might indicate the so-called sleeper effect that has been repeatedly demonstrated in LTPP, in which symptomatic change is brought about as a consequence of the gradual consolidation of internal changes and internalization of the analytic function a few years post-treatment (Abbass, Town, & Driessen, 2011; Leichsenring & Rabung, 2011). However, findings may

also be due to additional treatment, as 50% of Self-Critical Depressed in LTPP received an additional short-term therapy, compared with 33% of those in TAU.

As expected, individuals with Submissive and Dismissive Depression showed no sustained changes in depression severity after receiving LTPP or TAU, despite receiving substantial additional short-term treatment during the follow-up (over 40% of Submissive Depressed in both LTPP and TAU, and 28% and 11% of Dismissive Depressed in LTPP and TAU respectively). As Joyce and Piper (2007) have emphasized, entrenched personality issues that are persistent across the course of treatment are much more difficult to work with than those that occur more episodically and emerge as part of the therapeutic relationship. The more severe the problems with relatedness and self-definition, the more likely they are to have had a negative impact on the therapeutic process and the therapeutic alliance. A follow-up study will investigate this hypothesis. Yet, in general, these findings are consistent with studies suggesting that patients with lower levels of personality organization show worse outcomes (see Koelen et al., 2012 for a summary), and that more traditional LTPP may need considerable adaptation to be effective with these patients (Fonagy & Bateman, 2006; Levy, 2000). For instance, the personality features of individuals with Dismissive Depression may have led these individuals to distance themselves from the therapist and the treatment process, given their strong need for control and their highly critical stance toward others. The personality features of those with Submissive Depression, by contrast, may have interfered with treatment, in that their intense need to seek the therapists' approval might have hampered the establishment of a productive working alliance, and may have prohibited any attempt at independent thinking and adequate working-through of their problems and difficulties. However, it is important to point out that some individuals in both groups did show improvement during the early phase of the treatment period. At the 12-month time point, 44% of patients with Dismissive Depression in LTPP achieved CSC, compared with

17% of those receiving TAU. As Blatt (2004) speculated, as treatment progressed, interpretations offered by the therapist might have been perceived by these individuals as critical and authoritarian, provoking the Dismissive Depressed patients' tendency to get into power struggles. The more maladaptive anaclitic (Submissive) depressed individuals, on the other hand, appeared to benefit more from TAU than LTPP during the early phase of the treatment. It could be that the repeated activation, exploration, and interpretation of their typical patterns of thinking and feeling may have uncovered and enhanced their pervasive sense of inner badness and unworthiness. Patients in the Submissive Depression cluster share many features with patients with features of borderline personality disorder, and it might thus be that they struggle with the emphasis in LTPP on insight. Indeed, it has been argued that these patients could benefit more from therapeutic interventions that attend first to reactivating reflective capacities and de-emphasize insight, particularly in the early stages of treatment (Fonagy, Luyten, et al., 2015; Joyce & Piper, 2007; Piper et al., 2002). Again, further research is needed here. Patients in the Heterogeneous Group, finally, were not found to benefit from either LTPP or TAU. This contrasts findings reported by Shahar et al. (2013) who found them to benefit the most from LTPP. Although it is difficult to make any solid interpretation given the complexity of this group in the present study, it is of interest to note that they too had the highest estimated mean depression score over time compared with the other groups. In addition, these individuals may be characterized by a 'double vulnerability' with marked struggles involving both relatedness and self-criticism. This may be reflected in more severe and protracted pathology, rendering these individuals the most difficult to treat. By contrast, the mixed-individuals in Shahar et al.'s (2013) study seemed to be patients with less entrenched personality patterns. Indeed, recent studies concerning the general psychopathology or p-factor suggest that greater severity might be the best predictor of

treatment outcome (Caspi & Moffitt, 2018). However, more research is needed before any substantial conclusions can be drawn concerning this group of patients.

Study Limitations

The present results need to be interpreted within the context of several limitations. Most notably, while the statistical analyses benefited from the comprehensive and robust design of the TADS, assessment of the AIDA dimensions was done retrospectively and was thus not included in the trial design and power calculations. As a consequence, the subgroups contained relatively small samples and varied within and between the two treatment conditions. Given that the original trial was powered to compare differences between LTPP and TAU only, this might have precluded the detection of small but nevertheless meaningful effects. Second, the vast majority of the patients remained on antidepressants, and hence it is unclear whether the observed effects were due to psychotherapy, medication, or a combination of both. However, it is highly unlikely that antidepressant medication contributed to the observed post-treatment changes, as many of these patients had been on antidepressants for more than 10 years and had had at least two failed treatment attempts with antidepressants. Similarly, although additional psychotherapy seeking might also explain differences between the patient groups, there were no significant differences in this respect between the different groups of patients. Relatedly, time and treatment dose may be an important factor to take into account, as individuals in LTPP had a substantial higher dose of treatment compared to most individuals in TAU. Yet, the very different trajectories of change, even among the higher functioning patients, and the fact that these were all chronically depressed patients with a long history of depression, argues against a simple interpretation in terms of the passing of time and simple dose-response relationships. A follow-up study focusing on process-outcome relationships will address this issue. A third limitation pertains to the generalizability of the findings. The treatment modality investigated

may not be generalizable to other forms of psychoanalytic psychotherapy and therapists. Furthermore, future research should investigate the differential effect of the four derived dimensions of depression on a wider range of outcome measures. Another limitation pertains to the exclusion of therapist effects and the possible interactions between therapist and patient effects. As Crits-Christoph and Mintz (1991) argued, even small therapist effects, if not modeled, can bias statistical analyses. Ideally, these would have been included as a third level in the MLM; however, this would have required a larger sample size and a more equal distribution of the therapist: patient ratio.

Finally, in order to address the problem of missing data, the current study utilized an MI approach following Rubin's (1987) rule. Although this technique is an efficient and advantageous approach that has become popular (Allison, 2001), there remains a wide range of practical issues in need of consolidation and further development (Kenward & Carpenter, 2007). The present study followed the recommendation of Graham et al. (2007), and further research should aim to carry out a systematic sensitivity analysis to determine how many imputed data sets would be most sufficient (Kenward & Carpenter, 2007). Using this technique, various post-estimation methods are not directly applicable, and the appropriate MI versions are still in development. Thus, repeated ANOVAs or pre and post *t*-tests could not be calculated to determine effect sizes of the dimensional HRSD scores in the current study. Chi-square statistics to test for statistical differences between proportions could also not be carried out. However, the interested reader is referred to van Ginkel and Kroonenberg (2014), who recently suggested a definition for pooling F-tests of ANOVAs, which, once more widely accepted, might be included in mainstream statistical packages.

Conclusions

These findings have important implications for the treatment of treatment-resistant depression. This study found evidence for a differential treatment response among these

patients as a function of pre-treatment personality features. The findings seem to indicate that LTPP may not be modified enough to change the influence of the more problematic and maladaptive personality in the course of the treatment. Knowing in advance whether a patient possesses a particular anaclitic or introjective personality that manifests as their respective preoccupations with relatedness or self-definition at different developmental levels might inform treatment strategies. As such, in a next step we will examine more closely the treatment process of these patients in order to identify the specific therapeutic interventions used in relation to outcome.

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Table 1. Frequencies of drop-out and additional treatments for each AIDA Cluster

	Submissive		Dismissive		Self-Critical		Needy		Heterogeneous	
	LTPP	TAU	LTPP	TAU	LTPP	TAU	LTPP	TAU	LTPP	TAU
TADS Treatment Condition	LTPP	TAU	LTPP	TAU	LTPP	TAU	LTPP	TAU	LTPP	TAU
Sample Size	12	17	9	7	18	12	12	6	15	12
Drop-out (no data)	8%	6%	22%	29%	0	0	17%	17%	7%	0
Drop-out (lost to follow-up)	33%	18%	33%	0	5%	25%	8%	0	7%	8%
Additional Treatment during 18-months Treatment Period										
Psychodynamic	0	0	0	0	0	0	0	0	0	0
CBT	0	0	0	14%	0	25%	0	33%	0	8%
Counselling	0	18%	0	14%	0	17%	8%	33%	0	42%
Other Psychotherapy	17%	18%	22%	0	6%	0	0	0	13%	8%
Total	17%	35%	22%	29%	6%	42%	8%	67%	13%	58%
Total session number	22	163	78	26	7	71	6	73	30	154
Hospital Inpatient	8%	18%	0	0	0	0	8%	17%	7%	0
ADM	83%	100%	100%	71%	78%	100%	75%	83%	87%	67%
Additional Treatment during 2-Year Follow-up										
Psychodynamic	8%	0	0	0	0	0	8%	17%	0	8%
CBT	17%	12%	0	0	33%	33%	17%	0	7%	8%
Counselling	8%	6%	0	14%	6%	8%	8%	0	20%	17%
Other Psychotherapy	17%	30%	11%	14%	17%	0	8%	0	7%	8%
Total	42%	47%	11%	29%	50%	33%	33%	17%	33%	42
Total session number	131	208	24	13	101	65	440 ^a	52	92	101
Hospital Inpatient	33%	18%	0	0	6%	0	0	0	20%	8%
ADM	75%	82%	67%	57%	67%	75%	50%	50%	87%	75%

Note: ADM = antidepressant medication, CBT = Cognitive Behavioral Therapy, LTPP = long-term psychoanalytic psychotherapy, TAU=treatment as usual.

^a = the number is so high due to one patient receiving private 5-times a week psychoanalysis.

Table 2. Parameter estimates of the final linear growth model for each AIDA prototype

Fixed and random effects	Estimation based on 40 imputations exp(B) and (standard errors)				
	AIDA Reference group ¹				
	Submissive	Dismissive	Self-critical	Needy	Heterogeneous Group
AIDA and treatment effects of follow-up					
Intercept	12.57 (1.62)***	12.21 (2.10)***	7.50 (1.80)***	11.92***	14.53 (1.76)***
Treatment effect (LTPP, compared to TAU)	0.61 (1.72)	-2.76 (2.29)	-0.06 (1.67)	-5.76 (.2.26)**	-3.59 (1.74)*
<i>Group comparisons</i>					
Submissive x LTPP	REF				
Dismissive x LTPP	-3.37 (2.87)	REF			
Self-Critical x LTPP	-0.62 (2.41)	2.76 (2.84)	REF		
Needy x LTPP	-6.37 (2.86)*	-2.99 (3.21)	-5.75 (2.79)*	REF	
Heterogeneous x LTPP	-4.2 (2.45)	-0.82 (2.87)	-3.58 (2.41)	2.17 (2.83)	REF
Changes over time as a function of AIDA group					
Linear Time	-1.28 (0.26)***	-1.19 (0.33)***	-1.65 (0.28)***	-1.04 (0.35)**	-0.71 (-0.28)*
Quadratic Time	0.17 (0.03)***	0.17 (0.03)***	0.17 (0.3)***	0.17 (0.03)***	0.17 (0.03)***
<i>Group comparisons (of linear time effects only)</i>					
Submissive x Time	REF				
Dismissive x Time	-0.09 (0.32)	REF			
Self-Critical x Time	-0.37 (0.27)	-0.46 (0.33)	REF		
Needy x Time	0.24 (0.33)	0.15 (0.39)	0.61 (0.34)	REF	
Heterogeneous x Time	0.57 (0.26)*	0.48 (0.33)	0.94 (0.28)**	0.34 (0.35)	REF
Changes over time as a function of AIDA group and treatment					
Treatment group (LTPP) x Time	-0.22 (0.27)	-0.15 (2.29)	-0.03 (0.26)	-0.93 (0.35)**	-0.55 (0.27)*
<i>Group comparisons</i>					
Submissive x LTPP x Time	REF				
Dismissive x LTPP x Time	0.07 (0.45)	REF			
Self-Critical x LTPP x Time	0.19 (0.38)	0.13 (0.44)	REF		
Needy x LTPP x Time	-0.72 (0.45)	-0.78 (0.49)	-0.91 (0.43)*	REF	
Heterogeneous x LTPP x Time	-0.33 (0.38)	-0.39 (0.44)	-0.53 (0.37)	0.38 (0.44)	REF
Random effects					
Level 1: within-person	10.21 (1.63)				
Level 2: in initial status	15.66 (0.87)				

Note: LTPP = long-term psychodynamic psychotherapy. REF = reference group. Reference group for categorical variables are also shown in parenthesis after variable name.

* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$

¹Each column presents the same linear mixed model, re-parameterized so that model terms are with reference to each of the AIDA groupings.

Table 3. Observed depression severity and proportion of clinical significant change for each AIDA prototype by measurement point

AIDA group	Time Point	Observed pooled HRSD (means and severity category)				Clinical Significant Change (%)	
Submissive		LTPP		TAU		LTPP	TAU
	Baseline	22.42	severe	22.29	severe	0	0
	6 months	22.80	very severe	18.45	moderate	0	18%
	12 months	20.38	severe	17.88	moderate	0	24%
	18 months	20.02	severe	19.60	severe	0	17%
	24 months	19.48	severe	18.76	severe	0	18%
	30 months	21.82	severe	19.65	severe	8%	18%
	42 months	20.28	severe	20.17	severe	8%	6%
Dismissive		LTPP		TAU		LTPP	TAU
	Baseline	19.89	severe	21.00	severe	0	0
	6 months	16.37	moderate	18.90	severe	11%	14%
	12 months	14.01	moderate	16.16	moderate	44%	17%
	18 months	16.33	moderate	17.46	moderate	11%	14%
	24 months	16.08	moderate	17.24	moderate	11%	14%
	30 months	17.13	moderate	20.95	severe	11%	14%
	42 months	16.97	moderate	19.29	severe	11%	14%
Self-Critical		LTPP		TAU		LTPP	TAU
	Baseline	19.89	severe	19.92	severe	0	0
	6 months	15.91	moderate	16.04	moderate	6%	25%
	12 months	14.31	moderate	15.02	moderate	11%	25%
	18 months	14.82	moderate	14.27	moderate	17%	17%
	24 months	14.44	moderate	14.03	moderate	11%	25%
	30 months	15.38	moderate	14.28	moderate	6%	17%
	42 months	14.12	moderate	16.06	moderate	33%	17%
Needy		LTPP		TAU		LTPP	TAU
	Baseline	19.17	severe	18.33	moderate	0	0
	6 months	14.72	moderate	17.92	moderate	8%	17%
	12 months	17.75	moderate	16.59	moderate	0	17%
	18 months	14.64	moderate	17.07	moderate	22%	0
	24 months	11.91	mild	15.86	moderate	56%	0
	30 months	11.88	mild	19.35	severe	67%	0
	42 months	14.21	moderate	19.07	severe	25%	0
Heterogeneous		LTPP		TAU		LTPP	TAU

Baseline	18.80	severe	19.92	severe	0	0
6 months	17.48	moderate	17.49	moderate	7%	8%
12 months	17.94	severe	18.43	moderate	7%	8%
18 months	17.34	moderate	17.94	moderate	0	8%
24 months	16.17	moderate	19.16	severe	7%	0
30 months	18.97	severe	21.06	severe	7%	0
42 months	17.21	moderate	22.20	severe	7%	0

Note. CSC = clinical significant change, FU = follow-up; HRSD = Hamilton Rating Scale for Depression; LTPP = long-term psychoanalytic psychotherapy; TAU=treatment as usual.

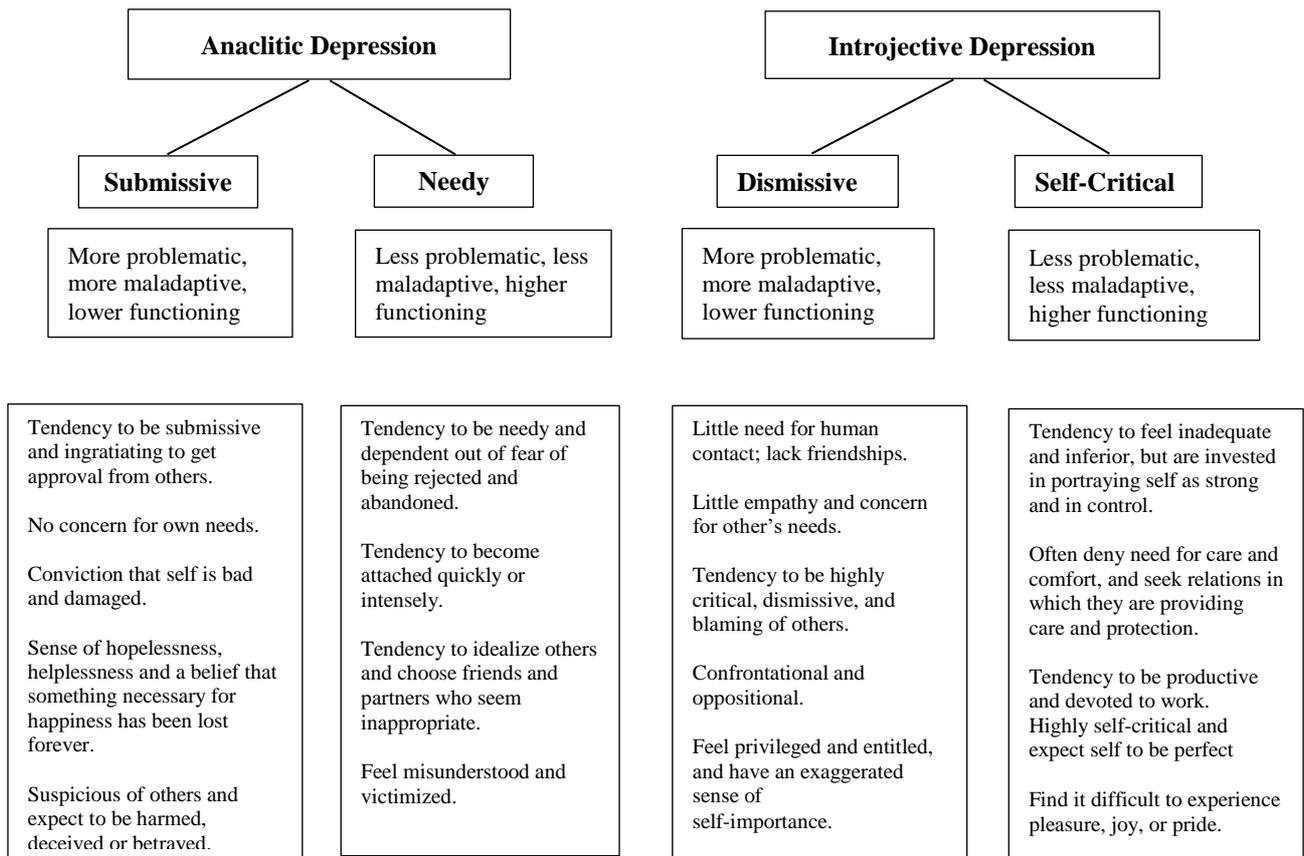


Figure 1. Summary description of the four AIDA clusters

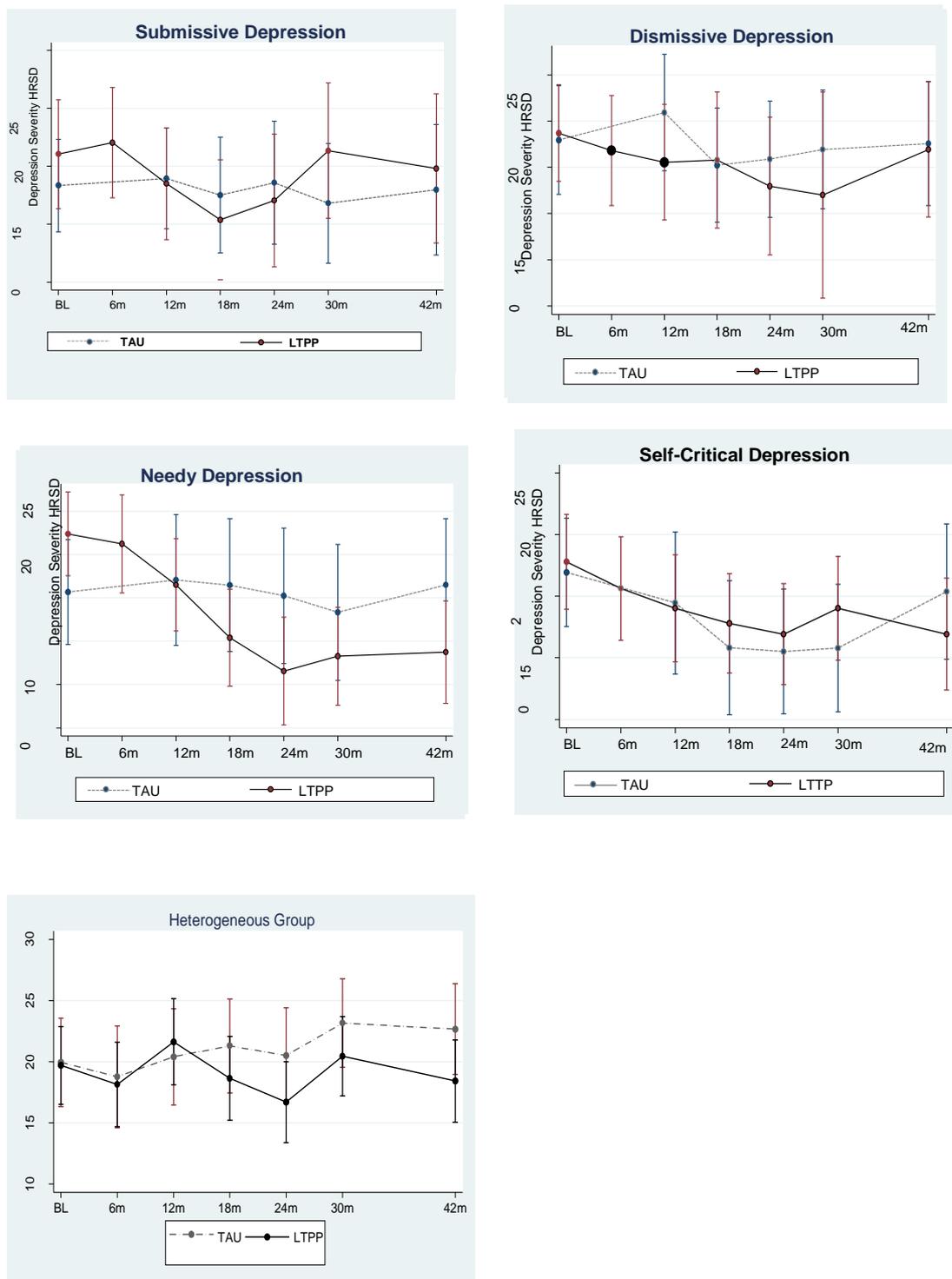


Figure 2. Depression trajectories as a function of treatment group for each AIDA prototype

Table for supplementary material

Appendix S1. Sociodemographic Characteristics across AIDA Group and Treatment Condition

Variable	Submissive		Self-Critical		Dismissive		Needy		Heterogeneous	
	<i>LTPP</i>	<i>TAU</i>	<i>LTPP</i>	<i>TAU</i>	<i>LTPP</i>	<i>TAU</i>	<i>LTPP</i>	<i>TAU</i>	<i>LTPP</i>	<i>TAU</i>
Sample size (%)	12 (18%)	17 (27%)	18 (27%)	12 (18%)	9 (14%)	7 (11%)	12 (18%)	6 (10%)	15 (23%)	12 (18%)
Gender (% female)	6 (50%)	14 (82%)	12 (67%)	10 (83%)	4 (44%)	2 (29%)	8 (67%)	3 (50%)	12 (87%)	9 (75%)
Age Mean (SD)	41.6 (7.5)	43.4 (8.7)	44.2 (11.2)	44.6 (13.8)	46.6 (11.1)	50.1 (6.4)	39.6 (9.9)	49.0 (11.2)	42.1 (12.1)	45.9 (10.2)
Ethnicity (white) (%)	10 (83%)	12 (71%)	15 (83%)	9 (75%)	9 (100%)	6 (86%)	7 (58%)	5 (83%)	13 (87%)	11 (92)
Relationship (% single)	11 (92%)	15 (88%)	11 (61%)	9 (75%)	9 (100%)	5 (71%)	9 (75%)	5 (83%)	14 (93%)	9 (75%)
Employment (% yes)	3 (25%)	1 (6%)	13 (72%)	8 (67%)	3 (33%)	2 (29%)	10 (83%)	4 (67%)	6 (40%)	1 (8%)
Education (% degree)	4 (33%)	6 (35%)	13 (72%)	6 (50%)	3 (33%)	3 (43%)	11 (92%)	3 (50%)	8 (53%)	3 (25%)
BL HRSD Mean (SD)	22.4 (5.1)	22.3 (4.5)	18.9 (4.6)	19.9 (3.9)	19.9 (5.4)	21.0 (3.9)	19.17 (6.0)	18.3 (3.9)	18.8 (4.7)	19.9 (6.3)

Note: BL = Baseline; HRSD = Hamilton Rating Scale for Depression, LTPP = long-term psychoanalytic psychotherapy, TAU=treatment as usual.

Appendix S2. Parameter estimates of the final linear growth model to test differences between LTPP and TAU in the TADS with 40 imputations

Fixed and random effects	Estimation based on 40 imputations exp(B) and (standard errors)
Fixed effects	
Intercept	11.99 (1.39)***
Education (university degree)	-2.21 (0.93)**
Treatment group (LTPP)	-2.30 (0.99)*
Growth rate depended on time	
Linear Time (42 months)	-1.19 (0.22)***
Quadratic Time	0.174 (0.3)***
Growth dependent on time and treatment group	
Treatment group (LTPP) x Linear Time (42 months)	-0.36 (0.15)*
Random effects	
Level-1: within-person	1.25 (0.51)***
Level-2: in initial status	19.25 (3.78)***
Level-2: in linear growth	0.22 (0.09)***

Note: FU = follow-up. LTPP = long-term psychodynamic psychotherapy. TAU = treatment as usual. Reference group for categorical variables is shown in parenthesis after variable name. * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$