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Patient Predictors of Response to Interpersonal Psychotherapy (IPT) for Depression

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Researchers in the past 20 years have identified a number of patient-specific variables that appear to moderate response to IPT for depression. These factors include length of the depressive episode, biological sleep profile, baseline social functioning, adult attachment profile, level of perfectionism, presence of personality disorder, level of somatic anxiety, and expectations about treatment. The therapeutic alliance is also important to consider, as it may interact with patient characteristics to influence outcome. The evidence for each of these factors is presented in order to begin to create a profile of patients who are more likely to respond to IPT for depression. Implications for clinical practice and future research directions are discussed.

The psychotherapy treatment literature provides evidence that a single treatment is not appropriate for all patients with the same disorder. Interpersonal Psychotherapy (IPT), a time-limited, manualized treatment that focuses on the relationship between depression and current interpersonal problems (Weissman, Markowitz, & Klerman, 2000), is no exception. Having established that IPT is a generally efficacious treatment for Major Depressive Disorder (e.g., Elkin et al., 1989), researchers have begun examining the characteristics of depressed patients for whom IPT is most appropriate. Though the literature in the area of patient-related moderators of response to IPT is in the early stages, some predictors of response have emerged. This research is important to consider for several reasons. Perhaps most valuable is this information's clinical utility in the selection of depressed patients suited to receive IPT. If certain characteristics of depressed patients can serve as markers of more likely IPT response, treatment decisions can be enhanced from the outset. An increased focus on response predictors may also further understanding about the mechanisms through which IPT exerts its ameliorative effects, thereby leading to enhancements in this valuable treatment.

In comparing results of the studies reviewed, it is important to consider the definition of "response" to IPT that is used. Many studies define response as "complete recovery" from the presenting depressive episode by the termination of treatment, operationalized via a cut-off score less than or equal to 6 or 7 on the 17-item version of the Hamilton Rating Scale for Depression (HRSD), an established, clinician-administered measure of depression symptoms (Hamilton, 1960). Other studies define response as remission from the current depressive episode, operationalized as a score of 7 or below on the HRSD for a number of consecutive weeks (usually 3 or 4). In addition to response to IPT, outcome is addressed in the research, defined as the continuous HRSD score at termination. Other studies include number of weeks to remission as an outcome variable of interest.

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Overview of Studies Reviewed

Many of the findings reviewed in this article are based on the National Institute of Mental Health (NIMH) Treatment of Depression Collaborative Research Program (TDCRP), a randomized, multi-site clinical trial comparing the efficacy of IPT, cognitive behavior therapy (CBT), imipramine hydrochloride plus clinical management (imipramine-CM), and pill-placebo plus clinical management for non-bipolar, non-psychotic depressed patients (Elkin et al., 1989). Subjects were adult outpatients with a diagnosis of a current major depressive episode and scores of 14 or higher on the HRSD. Treatment in each condition consisted of 16 to 20 sessions conducted over 16 weeks by experienced psychologists and psychiatrists trained to deliver treatment in accord with detailed manuals. Two hundred fifty subjects were randomized, 239 entered the treatment, and 162 completed the 16-week trial. All four treatments were effective in reducing depressive symptoms and improving functioning, with IPT and CBT as effective as imipramine-CM. IPT and imipramine-CM were significantly more effective than placebo in reducing depression severity as measured by the HRSD (Elkin et al., 1989).

Other findings reviewed here are from studies of outpatient maintenance IPT for recurrent unipolar depression conducted by Frank and colleagues (Feske, Frank, Kupfer, Shear, & Weaver, 1998; Cyranowski, et al., 2002). Subjects were experiencing at least a second episode of major depression and had scores of over 14 on the HRSD. Subjects received 12 to 24 weeks of IPT, ending when remission

(defined as 3 consecutive weeks with HRSD <= 7) was achieved, at the end of 24 weeks, or at patient dropout (the later two groups were classified as non-remitters). Additional findings in this article are taken from Brown and colleagues' randomized controlled trial of IPT, nortriptyline, or usual care for patients with DSM-III major depression recruited from internal medicine clinics and family health centers (Brown, Schulberg, Madonia, Shear, & Houck, 1996; Brown, Schulberg, & Prigerson, 2000). Subjects had scores of 13 or higher on the HRSD. All treatments lasted 8 months; IPT included 16 weekly sessions followed by 4 monthly continuation-phase sessions. Findings from several other studies of IPT are described as they appear in the review below. Note that studies of IPT used in combination with pharmacotherapy (e.g., Dew et al., 1997; Greenhouse, Kupfer, Frank, Jarrett, & Rejman, 1987; Reynolds et al., 1996) are not included in this review, as the impact of IPT versus the drug treatment on response is unclear.

Key Patient Predictors of IPT Response

Researchers in the past 20 years have identified a number of patient-specific variables that appear to predict response to IPT for depression. These factors include the severity, onset, and duration of the patient's depression, depression of the endogenous type, social functioning, marital status, adult attachment profile, perfectionism, personality disorder, anxiety, and expectations about treatment. The evidence for each of these factors is presented.

Features of Depression

Features of a patient's depression, such as severity, duration, and onset may impact response to treatment. Examining the role of depression severity in the TDCRP study, Elkin and colleagues (1989) found that patients classified as having more severe baseline depression (HRSD >= 20) and more impaired baseline functioning defined via the Global Assessment Scale (GAS <= 50) had significantly lower depression scores and a greater chance of recovery (HRSD <= 6) at termination in the IPT and imipramine-CM conditions compared to placebo. In contrast, Feske and colleagues (1998) found that greater baseline depressive severity and GAS functional impairment predicted non-response to IPT. Brown, Schulberg, and Prigerson (2000) similarly found that baseline depression severity and functional impairment did not predict recovery (HRSD <= 7) at 8-month termination for the IPT group. Regarding duration of the current depressive episode, Sotsky and colleagues (1991) observed that across all TDCRP treatment groups episodes of 6 months duration or more were correlated with greater post-treatment depression severity. Feske and colleagues (1998) similarly found that longer duration of the index episode of depression was associated with non-remission. Depression with greater acuteness of onset (less than 3 months) predicted less depression severity at termination for patients treated with IPT or imipramine-CM in TDCRP (Sotsky et al., 1991).

Endogenous depression—that is, depression that is less situational and more innate or biological in nature—has long been thought to respond better to somatic treatments than to psychotherapy (Prusoff, Weissman, Klerman, & Rounsaville, 1980). However, the findings regarding IPT's effect on endogenous depression are mixed. In a study of 96 acutely depressed ambulatory patients, Prusoff and colleagues (1980) found that subjects with endogenous depression defined by Research Diagnostic Criteria (RDC) responded poorly to IPT alone, but positively when IPT was combined with pharmacotherapy. Patients not meeting criteria for RDC endogenous depression responded well to IPT. In contrast, Sotsky et al. (1991) found that RDC endogenous depression predicted reduction in depression severity in the IPT group. Feske et al. (1998) similarly found that subjects who failed to remit with IPT were more likely to meet RDC criteria for non-endogenous depression. An additional analysis of TDCRP data by Sotsky in 1997 found that subjects with symptoms of atypical depression (mood reactivity, hypersomnia, hyperphagia, or weight gain) responded better to IPT and CBT than to imipramine-CM or placebo (cited in Weissman, et al., 2000).

Commenting on the disagreement in the literature about the role of endogenous depression in moderating IPT response, Thase and colleagues (1997) noted a general lack of consensus about the features that best define endogenous depression. They proposed that EEG sleep information could more accurately identify patients with biological disturbances characteristic of endogenous depression. In a study of 91 subjects with unipolar or bipolar II depression, they examined the predictive utility of EEG sleep profiles to outcome from IPT. Subjects received two nights of EEG sleep recording to measure REM latency, sleep efficiency, and REM density, factors that have reliably discriminated between depressed and healthy subjects in previous research. Subjects were then divided into two groups, one which met the profile for an abnormal sleep profile similar to depressed inpatients (n = 41) and the other with a normal sleep profile (n = 50). All subjects were treated with up to 16 weekly sessions of IPT. Subjects with abnormal sleep profiles had significantly poorer response to IPT as measured by HRSD ratings, treatment attrition, and depression remission (defined as 4 consecutive weeks with HRSD <= 7). Biologically disturbed patients appeared to respond poorly to IPT even though pretreatment depression severity did not impact outcome. The authors concluded that IPT may less effective for a subgroup of endogenously depressed patients (those with objective signs of neurobiological dysfunction), thus explaining the lack of agreement in earlier findings.

Social Functioning

IPT is based on the principle that depression can be treated by focusing on the interpersonal context (Weissman,

et al., 2000); thus, pretreatment social functioning might be expected to have an impact on IPT's outcome. Sotsky et al. (1991) found that less pretreatment social dysfunction, as measured by the 11-item social and leisure activities subscale of the clinician-administered Social Adjustment Scale (SAS), was associated with less depression severity and complete response across all four treatments at termination, but most markedly for IPT. Subjects with more severe social deficits responded poorly to IPT. Patients who had lower social dysfunction prior to treatment, higher interpersonal sensitivity, and higher satisfaction with interpersonal relationships tended to be more responsive to IPT. The authors theorized that patients might need a minimum baseline social functioning ability in order to respond well to IPT. In contrast, Feske et al. (1998) found that subjects who did not respond to IPT had higher levels of social functioning, as measured by the Social Attainment Scale, than those who did. Though these two studies used different measures of social functioning and different definitions of response, the discrepancy in their findings requires further research. Also of note, it has been found that subjects in the TDCRP who were divorced or separated responded better to IPT, whereas married patients responded better to CBT (Barber & Meunz, 1996). Marital status was not significantly related to IPT outcome in either the Feske et al. (1998) or Brown and colleagues (2000) studies. The relationship of marital status to social functioning in the prediction of response to IPT remains to be explored in detail.

Further investigating the role of social functioning, Cyranowski and colleagues (2002) reported data indicating that adults with insecure attachment styles may have poorer interpersonal functioning and higher vulnerability to depression. They described three patterns of adult insecure attachment—preoccupied, dismissing-avoidant, and fearful-avoidant—each with implications for interpersonal functioning. They examined data from 162 female participants with recurrent depression in Frank's study of maintenance IPT to explore the relationship of adult attachment status to treatment response. Attachment styles were measured by the self-rated Relationship Questionnaire. The authors found that though the proportion of subjects who remitted (HRSD <= 7 for 3 consecutive weeks) did not differ by attachment profile, among subjects who did remit (n = 87), those with secure attachment had significantly less time to remission (mean 8.5 weeks) than those with fearful-avoidant attachment (mean 13 weeks). In this sample, women with fearful-avoidant attachment profiles tended to have a more negative view of self and others, more trouble socializing, and more interpersonal difficulties. Although women with this profile responded to IPT in equal proportion to those who were securely attached, they responded more slowly. Though limited by its use of a self-report measure of attachment style, this study provides evidence that a brief course of IPT may not be enough time for fearful-avoidant patients to develop a trusting relationship.

Perfectionism

A series of studies examining TDCRP data has provided strong evidence for the damaging role of perfectionism on response to treatment. Authors using TDCRP data have assessed perfectionism via the Dysfunctional Attitudes Scale (DAS), a measure of cognitive dysfunction that assesses self-critical and socially dependent attitudes. Overall, TDCRP subjects with lower cognitive dysfunction as measured by the DAS tended to respond better to CBT and imipramine-CM than to placebo (Sotsky et al., 1991). Cognitive dysfunction did not predict IPT response. Using a principle-components analysis, Blatt, Quinlan, Pilkonis, and Shea (1995) identified two robust primary factors in the DAS: "need for approval" and "perfectionism." Pretreatment need for approval was not significantly related to outcome in any of the four TCDRP treatments, however, across treatments, high levels of pretreatment perfectionism predicted higher depression severity and more impaired functioning (GAS and SAS) at termination (Blatt et al., 1995).

A subsequent analysis found that the damaging effect of perfectionism on treatment outcome was consistent when response was measured at both termination and 18-month follow-up times and by clinical evaluators, patients, and therapists (Blatt, Zuroff, Bondi, Sanislow, & Pilkonis, 1998). The authors also found a temporal effect for perfectionism; though patients at all levels of perfectionism showed improvement from intake to mid-treatment, during the second half of treatment patients with moderate to high levels of perfectionism ceased improving, whereas those with low perfectionism continued to improve. Though the negative effects of perfectionism on outcome were seen across treatment types and not just in IPT, there is evidence that the adverse effects of perfectionism may be mediated by patients' satisfaction with social relationships (Shahar, Blatt, Zuroff, Krupnick, & Sotsky, 2004), and thus may be particularly relevant to IPT's focus on relationships. It seems that perfectionism contributes to difficulty in establishing the interpersonal relationships necessary for brief therapies such as IPT. However, these findings, all of which are based on TDCRP data and operationalize perfectionism by the DAS, require further replication.

Personality Disorder

Much research has indicated that patients with personality disorders have poorer and/or slower response to treatment for depression. Using TDCRP data, Shea and colleagues (1990) found that subjects with personality disorders, as diagnosed with the Personality Assessment Form (PAF) rated pretreatment by clinical evaluators, showed less improvement in social functioning at termination. Though no significant differences were found in HRSD outcome across treatments, there was a trend for subjects treated with IPT or imipramine-CM to have a better outcome when no personality disorder was present. In an extension of the above analysis, Shahar, Blatt, Zuroff, and

Pilkonis (2003) found that when personality disorder as measured by the PAF was treated as a continuous rather than a categorical variable, odd-eccentric cluster personality disorders (Cluster A; Paranoid, Schizoid, and Schizotypal) predicted worse outcome across treatments.

Bearden, Lavelle, Buysee, Karp, and Frank (1996) further explored the role of personality disorder on IPT response in their study of 76 subjects treated with 12 to 20 sessions of IPT. All subjects had a history of recurrent major depression, were currently experiencing a depressive episode of probable or definite endogenous subtype, and had baseline scores of 15 or above on the HRSD. The authors found that more total DSM-III diagnoses of personality disorders and more anxious-fearful cluster personality disorders (Cluster C; Avoidant, Dependent, and Obsessive-compulsive), as measured with the SCID Personality Disorders interview, predicted greater time to remission from depression (HRSD <= 7 for 3 consecutive weeks). A higher number of disordered personality traits and a rating of high personality disturbance versus low personality disturbance were related to longer time to respond to treatment. Brown, Schulberg, and Prigerson (2000) similarly found that patients receiving IPT who had a current DSM-III Axis II personality disorder were significantly less likely to recover.

Barber and Muenz (1996) provided further insight into the role of anxious-fearful personality disorders on response to IPT, examining the ways in which Avoidant Personality Disorder (AVPD) and Obsessive-Compulsive Personality Disorder (OCPD), as measured by the PAF, interacted with treatment to affect outcome in TDCRP subjects who received CBT or IPT. In accordance with their hypothesis, the authors found that IPT was more effective at reducing depression for subjects with OCPD whereas CBT was more effective with subjects with AVPD. The authors theorized that IPT may be better suited to obsessive patients because it uses internal coping strategies to motivate change. Avoidant patients who utilize more external coping strategies may not be well suited to IPT. A limitation in all studies described above, however, is that personality disorder was evaluated during the depressive episode, either at intake, or, in the case of Bearden et al. (1996), at four weeks into treatment. It is thus difficult to discern the effects of depression on personality from true Axis II personality disturbance.

Anxiety

Because depression is often comorbid with anxiety disorders, the influence of anxiety on response to treatment for depression is important to consider. Brown, Schulberg, Madonia, Shear, and Houck (1996) explored the role of lifetime anxiety disorders as measured by the Diagnostic Interview Schedule (DIS). Patients with a lifetime anxiety disorder presented with greater severity of depression, were more likely to drop out of the study, and showed less improvement over eight months when treated with either IPT or nortriptyline. Patients with depression alone, compared to patients with depression and anxiety, showed greater and more rapid reduction in symptoms, especially between intake and month four. Patients with comorbid anxiety tended to take twice as long to show similar reductions in depression severity. Looking at rates of full recovery (defined as HRSD <= 7), the researchers observed that IPT subjects with depression alone or with depression and lifetime generalized anxiety disorder were more likely to have recovered at four and eight months than subjects with depression and a lifetime panic disorder. These differences were not observed in the nortriptyline group. Feske et al. (1998) provided further evidence for the deleterious effect of anxiety disorders, and panic disorder in particular, on response to IPT. In their study of women with recurrent unipolar depression, treatment non-remitters (defined as HRSD >= 7 for 3 consecutive weeks) had significantly higher levels of somatic anxiety (measured by the HRSD) and were more likely to meet lifetime criteria for panic disorder (measured by the SADS or SCID) compared to treatment remitters. Total anxiety level as reported on the SADS and psychic anxiety as reported on the HRSD did not differentiate between remitters and non-remitters. It appears that IPT may effectively treat depression with some comorbid anxiety unless this anxiety is of a more somatic nature, as in panic disorder, in which case IPT is not as effective and pharmacotherapy may be warranted.

Expectations of Improvement

A final patient characteristic that has been studied as a predictor of response to treatment for depression, including IPT, is expectation of improvement. Across many types of psychotherapy, patients' expectations of improvement from treatment have been shown to be powerful predictors of outcome (reviewed in Meyer et al., 2002). Indeed, one of the ways in which IPT therapists may help patients recover from depression is by helping to increase expectations of treatment success by explicitly indicating that the outlook for recovery is good (Weissman et al., 2000). Findings from the TDCRP support the role of patient expectations in outcome (Meyer et al., 2002; Sotsky et al., 1991). Treatment expectancy in the TDCRP was assessed via a one-item measure administered at intake asking patients to rate their expectation of their outcome. Patient global expectancies, defined as status in one year assuming no other treatment, were also assessed with one item at intake. Researchers found that patient treatment expectations significantly predicted full recovery and reduction of depression symptoms across treatments with a medium effect size. Patient global expectancies, however, were not correlated with outcome (Meyer et al., 2002; Sotsky et al., 1991). A separate study conducted during the training of IPT therapists for the TDCRP found that negative patient expectations of outcome were correlated with greater hostile, defensive, and help-rejecting attitudes among patients, which in turn impeded therapists' ability to effectively administer IPT

(Foley, O'Malley, Rounsaville, Prusoff, & Weissman, 1987). This study provides support for the effects of patient expectations for outcome in IPT in particular. Perhaps related to expectations of outcome, Brown, Schulberg, and Prigerson (2002) found that patients who perceived more internal control over their health responded significantly better to IPT.

The Role of the Therapeutic Alliance

The therapeutic alliance is widely acknowledged as a key ingredient in effective psychotherapy across treatment types. In the TDCRP, stronger therapeutic alliances in early sessions and across all sessions, as measured variously by the evaluator-rated Vanderbilt Therapeutic Alliance Scale (VTAS) and the patient-report Barrett-Lennard Relationship Inventory (B-L RL), were strongly associated with less attrition and greater improvement in all treatment groups. In fact, more variance in outcome was attributable to the alliance than to the treatment method (Krupnick et al., 1996; Blatt, Zuroff, Quinlan, & Pilkonis, 1996).

Given the crucial role of the alliance on therapeutic outcome, it is not surprising that the alliance has been found to mediate and moderate several key patient predictors of response to treatment. For example, Meyer et al. (2002) found that the strength of the therapeutic alliance (as measured by the VTAS) appeared to mediate the relationship between patients' expectations and treatment outcome across treatments in the TDCRP. Patients with higher expectations of treatment outcome tended to develop stronger relationships with their therapists, which in turn led to a better outcome. Investigating the effect of perfectionism on the therapeutic relationship across treatments in the TDCRP, Zuroff and colleagues (2001) observed that the negative relationship between perfectionism and treatment response was partially mediated by the failure of perfectionists to develop stronger therapeutic alliances (measured by the VTAS) as therapy progressed. Blatt, Zuroff, et al. (1996) further noted that though quality of therapeutic relationship (measured by the B-L RL) was unrelated to outcome for patients with either very high or very low levels of perfectionism, it was associated with outcome for patients with moderate levels of perfectionism. In other words, for somewhat perfectionistic patients, a positive therapeutic relationship moderates the negative effects of perfectionism and helps to predict a better outcome. As seen in these preliminary studies of perfectionism and expectations of outcome, a patient's contribution to the therapeutic alliance may be one of the pathways through which patient characteristics affect outcome of treatment.

Clinical Applications and Directions for Future Research

This review has found evidence in the literature of several patient moderators of response to IPT for depression. Examining the data presented here, a profile of patients who may respond better to IPT emerges. It appears that to respond optimally to IPT as a treatment for depression, a patient should have a duration of the current episode of less than 6 months; a normal sleep profile; some minimum level of social functioning; an adult attachment style other than fearful-avoidant; less characterological perfectionism; lack of a personality disorder; lack of somatic anxiety symptoms or a lifetime diagnosis of panic disorder; positive expectations for the outcome of treatment; and more perceived internal control over health. Some of these characteristics, such as somatic anxiety and social functioning, appear to be specific factors affecting response to IPT in particular. Others, such as perfectionism and treatment expectations, are non-specific predictors of response across several types of treatment that have been shown to apply to IPT. Both specific and non-specific factors are important to consider in determining patients' likelihood to respond to IPT. Of additional importance in making treatment decisions are factors that have been found to differentiate IPT's effectiveness from that of other treatment options, including more severe depression (IPT may be better than clinical management alone); atypical depression (IPT may be better than pharmacotherapy); divorced or separated marital status (IPT may be better than CBT); and presence of Obsessive Compulsive Personality Disorder (IPT may be better than CBT). Of note, several variables seem consistently unrelated to IPT outcome, including age, gender, age of onset of first depressive episode, and number of previous depressive episodes (Brown, Schulberg, & Prigerson, 2000; Feske et al., 1998; Sotsky et al., 1991).

The clinical applicability of these findings in determining the "goodness of fit" for IPT and increasing particularly effective aspects of IPT (e.g., by further encouraging positive expectations of treatment outcome) is promising; however, more research in this area is needed. The research to date is limited by its dependence on one study, the TDCRP, for most results, with few findings replicated outside of this sample. The TDCRP was a well-designed study using highly trained, experienced therapists to deliver treatment. It is unknown whether predictors of response in the TDCRP would extend to IPT conducted by less experienced therapists in a less structured setting. It is noteworthy that the findings of other studies (e.g., Brown, Schulberg, & Prigerson, 2000; Feske et al., 1998) seem to conflict with the TDCRP findings in several respects. These contradictory findings may be due to differing populations studied, measures used, and/or definitions of response used; this requires further research. Additionally, the findings regarding non-specific predictors of response (e.g. perfectionism) require replication with studies addressing IPT treatment in particular.

The role of therapist characteristics in predicting response to IPT, alone and in interaction with patient variables, is another avenue for future research, especially in light of findings regarding the key role of the therapeutic alliance in predicting response to treatment. As yet there is

little data in this regard. However, preliminary research across TDCRP groups indicates that more effective therapists are not ones with more experience but rather with more psychological as opposed to biological orientations to the clinical process (e.g., they tended to favor psychotherapy over biological interventions for the treatment of depression) (Blatt, Sanislow, Zuroff, & Pilkonis, 1996). The implications of this finding for IPT have not yet been addressed. In conclusion, though some knowledge has been accumulated about patient predictors of response to IPT for depression, more research is needed to replicate and extend current findings. Additional research is also needed to focus on other potential predictors of response and on the interaction of established predictors with therapist and treatment variables.

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