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A Review of the Influence of Personality and Temperament on Major Depressive Disorder Treatment

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A Review of the Influence of Personality and Temperament

on Major Depressive Disorder Treatment

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Abstract

Researchers have developed multiple approaches to treat major depressive disorder (MDD). Clinicians commonly employ antidepressant medication (ADM) and psychotherapy as treatment protocols. This review surveys the knowledge and identifies problems with the effects of personality and temperament for MDD treatment in 14 quantitative studies. High extraversion and conscientiousness have a positive effect on psychotherapy treatment while high neuroticism has a negative effect. Agreeableness and openness to experience appear to have conflicting results. All individual traits do not influence ADM treatment except for high and low reward dependence, which may be better for psychotherapy and ADM respectively. Low persistence and high harm avoidance adversely affect psychotherapy, but novelty seeking has an insignificant effect. Some problems in the literature include the self-report measures for individual traits, heterogeneity of study designs, and the complexity of defining personality and temperament. This paper is limited to ADM by SSRIs, SNRIs, and tricyclic antidepressants. These findings may assist patients in choosing treatment types and clinicians in creating better treatment plans for patients, especially psychotherapy. This article may also contribute to the reconceptualization of mental disorders as a dimension instead of a type.

Keywords: Major depressive disorder, personality, temperament, antidepressants, psychotherapy

A Review of the Influence of Personality and Temperament

on Major Depressive Disorder Treatment

Only 41% of major depressive disorder patients (MDD) show a response to therapy

treatment (Cuijpers et al., 2021), and 60% fail to achieve complete remission (Kim et al., 2021).

MDD is a mental disorder characterized by depressed mood, loss of interest in activities, and

impairment of daily life for at least 2 weeks (Bains & Abdijadid, 2023). MDD reduces work

productivity, harms relationships, and predicts suicide ideation (Cai et al., 2021; Beck et al.,

2011; Vujeva & Furman, 2011). Knowing the influence of personality and temperament on

treatment can reduce the amount of time, money, and effort for recovery.

First, temperament is the variation of emotional reactivity determined by a person's

biology (Rettew & McKee, 2005). Cloninger's psychobiological model of temperament divides

temperament into 4 categories including harm avoidance (serotonergic function), reward

dependence (noradrenergic function), novelty seeking (dopaminergic function), and persistence;

an additional 3 traits relating to self-concept include self-directedness, cooperativeness, and

self-transcendence (Cloninger, 1993). To assess harm avoidance, reward dependence, and

novelty seeking, Cloninger (1991) created the Tridimensional Personality Questionnaire (TPQ).

Later, the Temperament and Character Inventory (TCI) was developed to account for persistence

and the 3 additional character traits, but the latter will be excluded for the purposes of a

manageable focus.

Second, personality is the set of traits that a person exhibits and changes more with

experience than temperament (Bergner, 2020). To define personality, the five-factor model of

personality (FFM) delineates five traits: neuroticism, extraversion, conscientiousness, openness

to experience, and agreeableness (McCrae et al., 1992). For assessment, the NEO Personality

Inventory-Revised (NEO PI-R) questionnaire analyzes personality traits with 30 sub-facets (6 facets in each of the 5 domains) (Costa, 2008; Rector et al., 2012).

After the development of the NEO PI-R, researchers found correlations between personality traits and mood states (Svrakic et al., 1992). Researchers started to explore the impact of personality, temperament, and personality disorders on treatment and recently its influence on mood disorders such as MDD (Reich & Green, 1991; Reynolds & Clark, 2001). Researchers developed tests to measure the severity of depression, which include the Hamilton Depression Scale (HDRS), Beck's Depression Inventory (BDI-II), and Montgomery-Asberg Depression Rating Scale (MADRS). MADRS and HDRS are structured interviews whereas BDI-II is a questionnaire, which may result in different measurement outcomes for participants; however, these are valid forms of measuring depression with similar scales of measurement (Brown et al., 1995; Heo et al., 2007). The goal of this review is to examine the impact of personality and temperament on psychotherapy and antidepressants for MDD. Clinicians may integrate these findings to enhance treatment, create better prognosis, and recommend treatment options based on individual traits.

Personality and Psychotherapy

Dermody et al. (2016) investigated whether personality traits impact interpersonal interactions with therapists and thus affect treatment in 49 MDD patients in cognitive behavioral therapy (CBT) and 54 patients in interpersonal psychotherapy (IPT) (65% female, 35% male, mean age of 41). The patients went through 16-20 weeks of therapy and completed HDRS, NEO PI-R, and the Impact Message Inventory to identify the depression severity, personality traits, communion with the therapist, and personal agency in participants. Higher extraversion, conscientiousness, and lower neuroticism (inverse relationship) predicted greater warmth from

the patient and thus better communion and treatment regardless of therapy approach. Contrarily, agreeableness is inversely related to agency and treatment outcome. The authors used 15 mediation models and combined CBT and IPT results for analysis, which may cause errors, but they used a strict criteria for significance to minimize this issue. However, the type of therapy can definitely affect the therapeutic outcome for the client. Personality was measured through self-report, but the results matched third-party informant observations, which have strong correlations (Miller et al., 2004).

Kushner et al. (2016) examined the effect of personality on therapeutic alliance in 209 people who participated in 16-20 weeks of therapy where 70 were assigned CBT, 74 to ADM, and 65 to IPT (63% female, 37% male, mean age of 40). The authors administered the BDI-II, HDRS, NEO PI-R, and the California Psychotherapy/pharmacotherapy Alliance Scales (CALPAS) questionnaire that assessed early and late therapeutic alliance. High neuroticism had a direct negative effect on outcome according to the BDI-II but not the HDRS. High agreeableness had an indirect positive effect on outcome in early and late therapeutic alliance. High extraversion and openness positively influenced late therapeutic alliance, but not overall outcome. The researchers utilized both BDI-II and HDRS to produce reliable measurements. However, they did not assess the personality and influence of clinicians on therapeutic alliance and results.

Thalmayer et al. (2018) inquired how the big six personality traits, which adds the honesty-propriety trait, the tendency for fairness and sincerity, influenced treatment usage and outcome in individuals, family, and couples therapy. The sample was 306 participants assigned to couples (46%), individuals (34%), family therapy (12%), or both individual and couples or family therapy (8%) (55% female, 45% male, mean age of 34.9). The types of therapy included

brief, strategic, solution-focused, emotionally-focused, or CBT, and the outcome questionnaire (OQ-45) measured psychological disturbances and progress in therapy. High extraversion and conscientiousness led to better outcomes in family and individual therapy, and low openness predicted a better outcome for individual clients. High neuroticism is related to a better psychological function and overall treatment outcome. The mental disorders treated were not only MDD but also a variety of problems, so the results may not be as strongly applicable to MDD. Finally, post-treatment data could be less accurate because more data was collected in the pretreatment than post-treatment.

Bagby et al. (2008) studied the interaction between personality and treatment type using CBT, pharmacotherapy (PHT), and IPT where 105 men and 175 women diagnosed with MDD completed HDRS, NEO PI-R, and 16-20 weeks of treatment (mean age of 41.9). Trial A had 36 in CBT, 38 in IPT, and 32 in PHT, and trial B had 69 in CBT and 37 in PHT. Selective serotonin reuptake inhibitors (SSRIs) prescribed included bupropion, citalopram, fluoxetine, paroxetine, phenelzine, and venlafaxine. High openness predicted lower depressive symptoms after treatment and high neuroticism predicted better results in PHT than CBT. In the agreeableness domain, lower trust, straightforwardness, and tender mindedness predicted better outcomes in PHT than CBT. The study produced strong results by implementing multiple trials with different forms of treatment. However, conclusions were not drawn from IPT because it lacked statistical power.

Analysis of Personality Traits in Psychotherapy

While two studies suggest a direction for neuroticism, one contradicts this trend, and the fourth compares two treatment types. High neuroticism predicted worse outcomes in therapy in Dermody et al. (2016) and Kushner et al. (2016). Neurotic patients experience more negative

affectivity and therefore struggle to recover. In addition, it is well-established that higher

neuroticism is correlated with higher risk of MDD and its severity (Duberstein & Heisel, 2007;

Xia et al, 2011). In contrast, Thalmayer et al. (2018) found that a higher neuroticism led to better

psychological functioning, but this could be an extreme outcome of regression towards the mean.

Personality could be measured incorrectly because some studies show that a depressive episode

during self-report can change scores in extraversion and neuroticism (Bagby, 1995).

For conscientiousness, two studies show a trend and the third shows a non-effect.

Although Dermody et al. (2016) and Thalmayer et al. (2018) find that high conscientiousness

leads to a better treatment outcome, Bagby et al. (2008) showed that conscientiousness did not

affect the outcome. The ability to complete tasks successfully is essential for outcome as therapy

is a strenuous process. Dermody et al. (2016) and Thalmayer et al. (2018) have participants who

are on average 30-40 years old, which means these findings may only apply to this age group.

For extraversion, two studies show a trend and the third shows a non-effect. Dermody et

al. (2016) and Thalmayer et al. (2018) suggest that high extraversion leads to a positive outcome.

The warmth from high extraversion can help a patient bond with the therapist. Kushner et al.

(2016) finds that extraversion does not have an effect in both therapy and ADM, but extraversion

did have a positive effect on therapeutic alliance similar to Dermody et al. (2016). High

extraversion has a positive impact on the therapeutic alliance, but this may not always lead to a

better outcome. Still, a strong therapeutic alliance allows a patient to share their thoughts and

feelings comfortably and this is essential to becoming self-aware and a better outcome (Arnow et

al., 2013; Falkenström et al., 2013).

For openness to experience, though two studies suggest openness is insignificant, one

study finds high openness as positive while another concludes that it is negative. Bagby et al.

(2008) finds that a high openness leads to a better outcome in CBT, IPT, and PHT, but Thalmayer

et al. (2018) finds the opposite in a variety of therapy approaches. Dermody et al. (2016) (only

CBT and IPT) and Kushner et al. (2016) hold that openness has an insignificant effect on therapy

and ADM. While Bagby et al. (2008) interprets that higher openness will lead to higher

treatment reception due to their tendency towards new experiences, people with low levels of

this trait may prefer the routine and familiarity of therapy. It would be ideal to replicate the

studies and examine the sub-facets in more detail because some sub-facets may be beneficial

while others could be detrimental.

Two studies find that high agreeableness has a negative effect, but one study concludes

that it is positive. Dermody et al. (2016) concludes that low agreeableness relates to a better

treatment outcome in IPT and CBT, but Kushner et al. (2016) and Bagby et al. (2008) finds that

it leads to a worse outcome. Dermody et al. (2016) explains that a low agreeableness is related to

higher agency and control over one's life, which enables a patient to take initiative and change

their life. Additionally, high agreeableness may hinder patient growth in therapy because high

agreeableness manifests as submissiveness and dependency. Low trust and straightforwardness

relates to the unwillingness to share one's feelings and thus harms therapeutic alliance (Bagby et

al., 2008). Therefore, PHT may be a better option for cynical patients. Since Dermody et al.

(2016) does not analyze sub-facets, this may explain the inconsistencies. For example, low trust

may harm the outcome while low altruism may benefit treatment because one focuses on their

needs instead of others.

Personality and Antidepressants

Petersen et al. (2002) used personality to predict treatment for fluoxetine (SSRI) in 76

depressed patients with a mean age of 40.5 (58% female, 42% male). The clinicians administered

10 mg/day in the first week, 4-20mg/day in week 2, 8-40 mg/day for week 5-8, 12-40 mg/day in week 9 to 12. Through the use of NEO PI-R and HDRS, the study revealed that personality did not predict outcome. However, the study had a small sample size and cannot be generalized other than fluoxetine.

Takahashi et al. (2013) investigated personality traits in 128 participants with MDD from Teikyo University Chiba center that include 27 remitted, 35 treatment-resistant (TRD), and 66 healthy patients for 8 weeks of ADM. The NEO-PI R and HDRS was used with an inclusion score of 14 and a remission score of 7 or less. TRD patients showed higher neuroticism and lower scores for extraversion, openness, and consciousness compared to the remission and the healthy group. Specifically, high scores in anxiety, depression, self-consciousness, and vulnerability in the neuroticism subset; low scores for warmth, gregariousness, assertiveness, activity, excitement-seeking, and positive emotion in extraversion; low feelings and action in openness; low competence, achievement, striving, and self-discipline in conscientiousness. The study does not report the specific ADM used for treatment, but they reinforce their findings by citing other studies and graphing data.

Analysis of Personality in Pharmacotherapy

Two studies find high neuroticism as negative while one study finds a non-effect. Although Kushner et al. (2016) and Takahashi et al. (2013) indicate the negative influence of high neuroticism on treatment outcome, Petersen et al. (2002) suggests that it does not affect outcome. Takahashi et al. (2013) does not specify the type of ADM used in its study, which may explain the different results because ADM tackles depression depending on its type. At the same time, this could be a minor effect because Takahashi et al. (2013) had a smaller sample size of TRD patients and Kushner et al. (2016) found an effect only by BDI-II not HDRS. Bagby et al.

(2008) implies that PHT is better for high neuroticism patients than CBT because patients, who are fatigued by negative emotions, require energy to use cognitive strategies as opposed to PHT. A combination of both may be optimal because patients can use PHT for the first couple weeks to re-energize and then change to CBT strategies, which has a lower recurrence rate of depression than PHT (Vittengl et al., 2007). High neuroticism is worse for clinical treatment in general but less harmful in ADM compared to psychotherapy.

For conscientiousness, two studies find a non-effect and one shows a negative effect from low conscientiousness. Kushner et al. (2016) and Petersen et al. (2002) illustrate that conscientiousness does not influence outcome. Contrarily, Takahashi et al. (2013) states that low conscientiousness has a negative effect on outcome. Petersen et al. (2002) uses fluoxetine (SSRI), but Kushner et al. (2016) and Takahashi et al. (2013) do not reveal the type of ADM in the study. The inconsistent results may be attributed to the missing specifications on the type and dosage of ADM. Takahashi et al. (2013) had 8 weeks of treatment when Kushner et al. (2016) and Petersen et al. (2002) had 12-16 weeks; conscientiousness may make a difference in the short term but not in the long term. Moreover, Takahashi et al. (2013) had a smaller sample size for TRD patients compared to the other two. Conscientiousness probably does not influence ADM because the efficacy is related to medication instead of the patient's actions. Thus, ADM may be a better option for patients with low conscientiousness because it requires less effort.

For extraversion, two studies find a non-effect and one shows a negative effect from low extraversion. Kushner et al. (2016) and Petersen et al. (2002) find that extraversion does not exert an influence on outcome. Nevertheless, Takahashi et al. (2013) suggests that low extraversion leads to a worse outcome, and Bagby et al. (2008) finds no difference between ADM and psychotherapy treatment. However, therapy may be more beneficial for people with

high extraversion because the nature of therapy and extraversion work effectively together. Extraversion may not be relevant to ADM because it involves minimal communication with the clinician. Few studies observed the relation between ADM and personality due to its weak relationship.

Two studies report a non-effect from openness, but one study reports an effect. Although Bagby et al. (2008) and Takahashi et al. (2013) predict a positive effect from high openness, Kushner et al. (2016) and Petersen et al. (2002) report an insignificant effect. Bagby et al. (2008) and Petersen et al. (2002) both use an SSRI called fluoxetine but find different results; the major difference is that Petersen et al. (2002) started with a lower dosage that increased over time when Bagby et al. (2008) had a fixed and larger initial amount prescribed. A higher concentration may explain the response in Bagby et al. (2008) and not Petersen et al. (2002). This means that openness may not have much of an effect as opposed to other factors such as ADM concentration.

Two studies report a non-effect from agreeableness, but one study reports an effect. Petersen et al. (2002) and Takahashi et al. (2013) report an insignificant effect from agreeableness except for Kushner et al. (2016). Agreeableness affects interpersonal interaction, but ADM does not involve interpersonal interaction. Still, Bagby et al. (2008) determines that PHT is more effective than CBT and IPT for high agreeableness participants, so conflicting data exists.

Psychotherapy and ADM combination

Hayward et al. (2013) investigated how personality influences the risk and treatment outcome of depression in 216 participants who were recruited at Duke University Medical center (60 years or older). 112 depressed and 104 non-depressed patients went through 12 weeks of

psychiatric treatment (both ADM and psychotherapy) and completed the NEO PI-R at the

beginning and MADRS every 3 months. Lower depressiveness and stress vulnerability, two

sub-domains of neuroticism, predicted a better outcome. Higher warmth and competence, a

sub-domain of extraversion and conscientiousness respectively, forecasted a better outcome.

Since the study consists of psychiatric patients and community volunteers, the positive results

may be skewed to the healthy group because they had the willingness to participate in the study.

Quilty et al. (2008) investigated the interaction between personality and treatment

outcome in 649 MDD patients who were recruited in Paris, France (66.9% female, 33.1% male,

mean age of 39.81) with an inclusion score of 20 on the MADRS. Participants were treated with

a combination of pharmacotherapy, tianeptine or fluoxetine, or psychotherapy, psychodynamic

therapy or supportive therapy, for 6 months. Patients received 50 mg/day of tianeptine (atypical

antidepressant) or 20 mg/day of fluoxetine, and a response was defined as a 50% reduction in

MADRS score. Higher openness, extraversion, conscientiousness and lower neuroticism

predicted more responses. Moreover, the study highlighted interactions between traits: high

conscientiousness and extraversion led to a better outcome; high neuroticism and extraversion

conduced towards a weaker response from ADM; high agreeableness and conscientiousness

predicted a better outcome. The study has a large sample size to avoid sample error, but the strict

exclusion criteria limited the results' external validity.

Combination of Psychotherapy and Pharmacotherapy

Although combined treatment may obfuscate the distinction between treatments, it offers

an alternative approach to treating MDD. Both studies find that high neuroticism is worse for

outcome; this is consistent with the negative effect of neuroticism on treatment in general. This

consistency is also seen in conscientiousness and extraversion where high levels of each trait

conduces a positive outcome. Hayward et al. (2013) reveals that the subfacet "competence" and "warmth" is significant compared to the other 5 subfacets in each trait. However, this consistency is not found in openness where Quilty et al. (2008) finds that a high openness predicts a better outcome and Hayward et al. (2013) finds it non-predictive. In addition, agreeableness does not affect the outcome according to both studies. The multidirectional effect of agreeableness can explain the conflicting results and consequent non-effect. The combination of ADM and therapy may complicate the results, but these results still support the consistency reported earlier.

Interactions of Personality Traits

Quilty et al. (2008) finds trait combinations predict certain outcomes in CBT and PHT treatment. High conscientiousness and extraversion together forecasted a better outcome because these people had a strong therapeutic alliance with their sociability and industriousness. However, high neuroticism and extraversion resulted in a worse outcome because it externalized neurotic traits such as active or passive avoidance. High agreeableness and conscientiousness predicted a better response due to higher trust and communication from the patient. There were few studies that explored the interactions between traits, but these interactions may reframe how researchers view the impact of personality traits by evaluating outcome based on multiple dependent interactions instead of individual traits. For instance, high extraversion predicted a better outcome when paired with high conscientiousness, but high extraversion led to a worse outcome when matched with high neuroticism. This is similar to how psychologists view the interaction of genes and environment together in behavior instead of independently (Ottmann, 1996).

Temperament and Psychotherapy

Joyce et al. (2007) find how personality disorder and temperament affect IPT and CBT treatment in a sample of 167 participants where 80 were randomly assigned to CBT and 87 to IPT for 16 weeks (72% female, 28% male, mean age of 35.2). According to the MADRS and TCI, high harm avoidance, low reward dependence, and low novelty seeking lead to a weaker outcome in IPT, and low persistence negatively affects CBT outcome. The researchers controlled for multiple variables and randomized the groups. The study was done for only 16 weeks, which means the results may not apply to long-term treatment (12-18 months). Many studies combine and analyze IPT and CBT together; however, this study compares the two different therapies.

Kronström et al. (2011) explored the predictive value of TCI on major depression from 35 participants in Finland (mean age of 42.7 years). 19 participants were assigned to psychodynamic therapy and 16 were prescribed 20-40 mg of fluoxetine for 16 weeks with HDRS and TCI as measurement instruments (inclusion score of 15). High reward dependence, self-directedness, and cooperativeness predict higher depressive scores after 4 months of fluoxetine, but this was not present in psychotherapy. This study has a small sample size and does not report temperament scores, so readers must trust the authors statements.

Analysis for Temperament in Psychotherapy

One study finds an effect for harm avoidance, but the other shows a non-effect. Joyce et al. (2007) finds that high harm avoidance negatively affects IPT but not CBT. People with high harm avoidance struggle with uncertainty, and IPT involves changes in the patient's social life. Moreover, high harm avoidance is considered a risk of depression (de Winter et al., 2007; Kampman et al., 2012). CBT explores cognitive strategies against negative thought patterns (Cognitive Behavioral Therapy, 2016); this involves more internal change than external and

environmental, which may make CBT easier because it involves change with oneself instead of multiple people. Kronström et al. (2011) does not find a significant effect from harm avoidance in psychodynamic therapy, which focuses on building internal resources by understanding how past events affect their present emotions (Center for Substance Abuse Treatment, 1999). Therapy that involves less external change may be more suitable for patients with high harm avoidance, but this may apply to change in general, in which case high harm avoidance patients may struggle in therapy.

One study finds an effect for reward dependence, but the other shows a non-effect. Joyce et al. (2007) suggests that low reward dependence predicts a worse outcome in IPT but not CBT. Low reward dependence is characterized by interpersonal deficit, which may hinder IPT progression because it focuses on fixing mood disorders through improving relationships and social functions. An alternate interpretation may be that IPT assumes that the root of depression derives from interpersonal contact, but these people may not seek this in the first place. On the other hand, CBT focuses on changing negative thoughts patterns instead of interpersonal relationships. Similar to CBT, Kronström et al. (2011) finds that reward dependence does not affect psychodynamic therapy because it involves less interpersonal interaction than IPT. Low reward dependence patients may have a better prognosis in CBT and psychodynamic therapy than IPT.

One study reported an effect from novelty seeking but the other found a non-effect. Joyce et al. (2007) found that low novelty seeking predicted a poorer treatment outcome in IPT but not CBT, but Kronström et al. (2011) found that novelty seeking did not impact psychodynamic therapy. Psychotherapy may be weak for low novelty seeking patients because they are averse to change in therapy.

Both studies find a negative effect of low persistence. Low persistence negatively influenced the treatment in CBT but not IPT and psychodynamic therapy according to Joyce et al. (2007) and Kronström et al. (2011). CBT involves confronting negative emotions and results in fatigue; higher persistence may help clients persevere through the challenging process of therapy. In fact, a study has found that affective temperament relates to resilience, which acts as a protective factor against depression (Kesebir et al., 2013). There are not many studies relating temperament and therapy outcome because the TCI dimensions relate to specific neural systems, so it makes more sense to connect ADM to temperament since they both concern a person's biology.

Temperament and Antidepressants

Newman et al. (2000) examined the influence of TCI on fluoxetine treatment of 199 MDD outpatients (55% female, 45% male, mean age of 40) who were assessed with the HDRS (inclusion score of 16) and TPQ. Receiving 20 mg/day of fluoxetine for 8 weeks, none of the traits had a significant effect on outcome. Although this study had a substantial sample size, it lacked a control group for comparison. Harm avoidance was also reduced throughout the trial, showing that temperament can change during treatment.

Joyce et al. (1994) examined the effects of TCI traits on treatment by clomipramine and desipramine (tricyclic antidepressants) in 84 depressed patients who completed 6 weeks of ADM treatment and the TPQ and HDRS (inclusion score of 14). At 2 weeks, the mean dosages for clomipramine and desipramine were both 122 mg, 135 mg and 171 mg respectively at 4 weeks, 144 mg and 199mg at 6 weeks. Temperament explained 35% of variance in the whole sample and 50% in severe patients. In women, high reward dependence and harm avoidance indicated a better clomipramine and desipramine response respectively. Low reward dependence, novelty

seeking, and harm avoidance together led to a better general response. High reward dependence and harm avoidance together led to a better response, but patients with high harm avoidance and low reward dependence conjointly did less well in treatment. Independently, these traits may have an insignificant influence on outcome. The study used self-report measures, but it explored tricyclic antidepressants that other studies do not often examine.

Nelson and Cloninger (1997) investigated the influence of temperament on nefazodone (SNRI) treatment and 1119 patients were recruited with 427 men and 692 women (mean age of 47.2) who completed the HDRS and TPQ. 100 mg of nefazodone was prescribed twice daily and adjusted within 100-600 mg/day for 8 weeks. Temperament predicted 1.1% variance of the HDRS change, where only high reward dependence predicted a lower response. The study lacked a control group to compare the results, but it has the largest sample size among all the studies.

Balestri et al. (2019) examined the effect of TCI dimensions on treatment. A sample of 743 patients was recruited from 6 European studies consisting of 455 with MDD and 288 with bipolar disorder (BPD) in ADM treatment who also completed the TCI and the HDRS and MADRS. Remission was assigned to participants who received a HDRS score 7 or lower; responders had at least a 50% reduction in HDRS or MADRS score after one treatment trial; treatment-resistant was classified as a decrease in score less than 50% after two treatment trials. Non-remission was related to high harm avoidance, self-transcendence, low persistence, and self-directedness, and non-responders had high harm avoidance, low reward dependence, and low self-directedness; treatment-resistant showed low reward dependence, persistence, and cooperativeness. The study has a large sample size and produces findings in non-remission,

treatment-resistant, and non-responders. However, the sample was collected from sites with different designs and purposes.

Analysis for Temperament in Pharmacotherapy

Three studies find a non-effect from harm avoidance, but one study finds an effect. Kronström et al. (2011) and Newman et al. (2000) suggest that high harm avoidance did not influence fluoxetine treatment and the same is concluded with nefazodone in Nelson and Cloninger (1997). According to Joyce et al. (1994), harm avoidance alone did not influence clomipramine treatment, but high harm avoidance predicted desipramine response in women. Nevertheless, Balestri et al. (2019) found that high harm avoidance led to non-remission and non-responders. High harm avoidance is related to excessive worrying, pessimism, and fatigue (Chen et al., 2015). Doubt and pessimism could have a negative effect on outcome as studies describe that the placebo effect plays a significant role in ADM treatment (Kirsch, 2014). Still, most of the studies show that harm avoidance does not affect outcome. Hence, ADM may be suitable for high harm avoidance patients because of its adverse effect on therapy.

Three studies find an effect from reward dependence and one study finds a non-effect. Kronström et al. (2011) and Nelson and Cloninger (1997) discover that fluoxetine and nefazodone respectively led to less response in high reward dependence patients. High reward dependence patients are sensitive to social approval and support, and ADM may not provide a space for this support. Since therapy does not affect high reward dependence patients, therapy may be better for high reward dependence patients. Joyce et al. (1994) shows that high reward dependence predicts better outcomes by clomipramine in women, but all the other studies do not show any influence of gender on ADM treatment outcome, so this may result from error. Newman et al. (2000) determines that reward dependence did not affect fluoxetine treatment, and

therefore a decisive conclusion cannot be made unless reward dependence is studied under

similar study designs. Joyce et al. (1994) finds that temperament explained 35% variance in

response and 50% variance in severely depressed patients. On the other hand, Nelson and

Cloninger (1997) finds that only 1.1% of variance in HDRS score is attributed to temperament;

this means that temperament may only slightly influence overall outcome, and time may be

better spent researching other factors. Nelson and Cloninger (1997) may have more validity

because it has a larger sample.

      All four studies find a non-effect from novelty seeking. Kronström et al. (2011), Newman

et al. (2000), Joyce et al. (1994), and Nelson and Cloninger (1997) find that novelty seeking

alone does not impact outcome regardless of the ADM type. Novelty seeking relates to people's

bias or initiation of behavior (Joyce et al., 2007). Where therapy may involve changing one's life

through action, novelty seeking does not influence how patients respond to medication. The

studies together suggest that ADM is a superior option for low novelty seeking patients because

they are less willing to confront unfamiliar situations in therapy.

      Three studies find a non-effect from persistence, but one study finds an effect. Kronström

et al. (2011), Newman et al. (2000), and Nelson and Cloninger (1997) find that persistence does

not affect outcome by fluoxetine and nefazodone, and yet Balestri et al. (2019) discerns that low

persistence conduces to non-remission and treatment-resistance but not non-responders.

Remission takes longer to achieve because it signals that the patient is recovering back to

normal. Patients with low persistence may not have the perseverance to reach remission as

opposed to receiving a response (a 50% reduction in HDRS score). Persistence does not affect

ADM outcome because it is unrelated to reactions that occur in the brain. However, persistence

can influence whether a patient consistently takes their ADM, but all the studies in this review

assume that participants follow the ADM schedule. Hence, the controlled nature of experiment may ignore the influential factors that would be seen in a real clinical situation. In fact, research has indicated the importance of compliance in ADM treatment (Cohen et al., 2004).

Conclusion

Clinicians can easily form a false impression of a person's personality due to cognitive biases such as the "halo effect" (Asch, 1946). Personality assessments may inform clinicians how to treat a patient; for instance, a therapist could provide more social support to clients with high reward dependence. Clinicians can focus on reducing the stress from high harm avoidance and neuroticism by suggesting coping skills specifically for these patients. For example, mindfulness is effective for people with high neuroticism (Drake et al., 2017). Extraversion and conscientiousness have a positive influence on therapy treatment while neuroticism has the opposite effect. Agreeableness and openness results show frequent inconsistencies, so further research that examines the effect of each sub-facet is warranted to elucidate differences. Personality does not affect ADM treatment due to the lack of connection. Other factors such as placebo may be a more auspicious area of research. Similar findings are found in temperament traits as harm avoidance, novelty seeking, and persistence does not affect ADM treatment. Hence, personality and temperament may not have much of an effect on ADM treatment. If temperament and ADM relate to neural systems, they should be an effect; therefore, research evaluating the efficacy of the TCI and ADM types may be justified.

Problems exist in the literature: self-report measurements for personality are dependent on memories, which are easily malleable and deceptive (Loftus, 2003). Moreover, completing the questionnaire during a depressive episode can influence results relating to depressive style or behavior (Hirano et al., 2002; Joffe et al., 1993). Subjective measures should supplement

objective instruments as even some researchers objectively analyzed temperament in early infants (Planalp et al., 2017). The definition and measurement of temperament and personality is divisive with studies arguing to implement a six factor personality model or personality styles (Jackson et al., 1996; Parker & Crawford, 2009). As long as this persists, the research question cannot be fully answered. The heterogeneity of study design burdens the comparison of articles. Some studies have different treatment strategies with varying dosage of ADM and types of therapy. Not to mention that factors such as past experiences, demographic background, and other factors can outweigh the influence of traits. Recovery can be misattributed to confounding variables instead of traits.

This article analyzes SSRIs, SNRIs, and tricyclic antidepressants but not other ADM such as dopaminergic reuptake blockers. Group therapy can also be explored because finding people with similar traits may lead to better outcomes (Ogrodniczuk et al., 2003; Ogawa et al., 2023; Pan et al., 2017). The findings do not extend to long-term, comorbid, or persistent depression disorder (Paavonen et al., 2016; Hellerstein et al., 2019).

Similar to medical diagnoses, researchers argue that the DSM-V can classify mental illness as a dimension instead of binary. Some argue that FFM can describe personality disorders more precisely and suggest treatment focused on neuroticism (Barlow et al, 2014; Widiger & Presnall, 2013). High neuroticism is adverse for MDD treatment, which implies that traits can contribute to the range of severity and symptomatology for MDD. The World Health Organization ranked depression as the 4th cause of burden of disease worldwide (Reddy, 2010). Patients have an abundance of treatment options and individual traits could help patients optimize their treatment and clinicians to enhance treatment plans.

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