Title
Personalized assessment and treatment of depression

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Personalized assessment and treatment of depression
Aaron J Fisher and Hannah G Bosley

The drive to personalize the delivery of psychosocial and pharmacologic treatments is embodied in Gordon Paul’s (1967) famous question, ‘What treatment, by whom, is most effective for this individual with that specific problem, and under which set of circumstances?’ Traditionally, researchers have examined ‘what works for whom’ via post hoc moderator analyses. However, these efforts have been largely unsuccessful, suffering from poor replication and statistical bias due a lack of random assignment. Recent advances in genetic and biological technologies and statistical methods have facilitated an explosion of research on the personalization of treatment for psychological disorders. The present review examines recent developments in the personalization of depression treatment.

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Research has consistently shown that treatments for depression are effective, with one meta-analysis demonstrating an average response rate of 54% across empirically supported treatments such as cognitive-behavioral therapy (CBT), interpersonal psychotherapy (IPT) and pharmacotherapy [1]. In the United States, depression has a lifetime prevalence rate of 13% [2], with approximately 15% of depressed individuals suffering from unremitting or recurrent depression — even after multiple treatment approaches [3]. Thus, although treatments for depression are generally effective, there is ample room to improve both the initial efficacy and long-term maintenance of treatment gains. The personalization of treatment design and implementation represents an exciting and burgeoning area for improving outcomes in depression.

Currently, ‘Strategy 3.2’ of the National Institute of Mental Health’s (NIMH) Strategic Plan [4], calls for mental health researchers to ‘expand and deepen the focus to personalize intervention research.’ As well, investigators have called for an increased emphasis on idiographic research [5,6] and the director of NIMH has called for research that can ‘transform diagnostics and therapeutics’ [7]. In medicine, the tailoring of interventions to individual needs is referred to as ‘personalized medicine’ and it has received a great deal of recent attention from the National Institutes of Health and the Food and Drug Administration [8]. Personalized medicine assumes that variability in treatment outcomes results from idiosyncratic initial conditions (e.g. genetic profiles) among individual patients [8]. The expectation is that identifying patterns of variation at the individual level will yield actionable, prescriptive information about which interventions are best-suited to which patients. Nevertheless, much work remains to be done. A recent systematic review and meta-analysis of clinical trials concluded that the present literature is insufficient to draw meaningful conclusions about personalized treatment for depression [9].

The present review addresses the current (and recently expanding) literature on personalized assessment and treatment of depression, with the ultimate goal of encouraging further research in this domain.

Biological factors: genetics, biomarkers, and medications
Personalized medicine — the use of molecular genetic analysis for selecting and implementing targeted treatments — is a fast-growing area of research for optimizing depression treatment. A burgeoning body of recent literature has explored the role of genetics in the symptom trajectories and treatment outcomes of major depressive disorder (MDD). With recent advances in technology that enhance accessibility to genetic sequencing and analysis, studies have taken off in multiple directions to investigate implications of genetics and other biomarkers in relation to personalized assessment and treatment of depression. Although a recent genome-wide association (GWA) study of 2431 MDD patients and 3673 controls failed to identify a single genetic mechanism or pattern that predicts MDD diagnosis [10], research has begun to examine the relationships between genes and treatment efficacy, indicating possibilities for personalized care. Table 1 provides a summary of recently identified candidate genes and their proposed functional roles.

Pharmacogenetics
The targeted employment of pharmacologic interventions for individuals with specific genetic profiles has been a major point of focus. Mitjans et al. [11] demonstrated that
<table>
<thead>
<tr>
<th>Paper(s)</th>
<th>Gene</th>
<th>Chromosomal locus</th>
<th>SNP</th>
<th>Function of gene</th>
<th>Relationship between gene and depression</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adkins et al. (2012), Domschke et al. (2013)</td>
<td>DRD4</td>
<td>11p15.5</td>
<td>na</td>
<td>Dopamine receptor</td>
<td>Although data are equivocal, there may be an association between the DRD4 gene and unipolar depression. Also, potential risk for psychotic symptoms</td>
</tr>
<tr>
<td>Adkins et al. (2012), Domschke et al. (2013)</td>
<td>DRD2</td>
<td>11q</td>
<td>rs1800497</td>
<td>Dopaminergic function, related to D2 receptor density</td>
<td>Certain alleles of this SNP are possible risk factors for affective disorders and increased risk of psychotic symptoms in depression</td>
</tr>
<tr>
<td>Domschke et al. (2013)</td>
<td>Unclear</td>
<td>1q42, 22q11, 19p13</td>
<td>na</td>
<td>(Multiple genes)</td>
<td>Potential risk loci of schizoaffective disorder</td>
</tr>
<tr>
<td>Domschke, et al. (2013)</td>
<td>Unclear</td>
<td>6p, 8p22, 10p13-12, 10p14, 13q13-14, 13q32, 18p, 22q11-13</td>
<td>na</td>
<td>(Multiple genes)</td>
<td>Potential risk loci of depression, bipolar disorder, and schizophrenia</td>
</tr>
<tr>
<td>Domschke et al. (2013), O’Leary et al. (2013)</td>
<td>DBH</td>
<td>9q34</td>
<td>na</td>
<td>Dopamine beta-hydroxylase: converts dopamine to norepinephrine</td>
<td>Increased risk of psychotic symptoms in depression</td>
</tr>
<tr>
<td>Domschke et al. (2013)</td>
<td>DTNB1</td>
<td>6p22.3</td>
<td>na</td>
<td>Protein-encoding gene necessary for the production of lysosomal organelles</td>
<td>Increased risk of psychotic symptoms in depression; may mediate antidepressant treatment response in psychotic depression</td>
</tr>
<tr>
<td>Domschke et al. (2013)</td>
<td>GSK-3 beta</td>
<td>3q13.3</td>
<td>na</td>
<td>Encodes for a protein called serine–threonine kinase involved in neuronal cell development and energy metabolism</td>
<td>Increased risk of psychotic depression</td>
</tr>
<tr>
<td>O’Leary et al. (2013)</td>
<td>CYP2D6, CYP2C19</td>
<td>22q13.1, 10q24</td>
<td>na</td>
<td>Pharmacokinetic genes related to how antidepressant drugs are metabolized by the liver (specifically, proteins from cytochrome P450 family)</td>
<td>Variants of this gene, resulting in ultra-rapid metabolism of antidepressants, could lead to reduced efficacy of these drugs</td>
</tr>
<tr>
<td>O’Leary et al. (2013)</td>
<td>ABCB1</td>
<td>7q21.12</td>
<td>rs2032583, rs2235015</td>
<td>P-glycoprotein is a membrane-bound multidrug resistance protein. Acts as ‘gatekeeper’ to the brain</td>
<td>Certain variants can reduce the absorption of antidepressant drugs</td>
</tr>
<tr>
<td>O’Leary et al. (2013), Domschke et al. (2013)</td>
<td>TPH1</td>
<td>11p</td>
<td>rs18000532</td>
<td>Tryptophan hydroxylase: rate-limiting enzyme for synthesis of serotonin from tryptophan</td>
<td>Certain alleles associated with decreased response to SSRIs; may mediate antidepressant response</td>
</tr>
<tr>
<td>O’Leary et al. (2013)</td>
<td>TPH2</td>
<td>12q21.1</td>
<td>rs10897346, rs7305115</td>
<td>Tryptophan hydroxylase: rate-limiting enzyme for synthesis of serotonin from tryptophan</td>
<td>Lacking the C allele of the first SNP results in decreased SSRI response; presence of the G allele of the second SNP improves SSRI response</td>
</tr>
<tr>
<td>O’Leary et al. (2013), Adkins et al. (2012), Domschke, et al. (2013), Landro et al. (2014)</td>
<td>SLC6A4</td>
<td>17q11.2</td>
<td>rs25531</td>
<td>Serotonin transporter (SERT), removes serotonin from synaptic cleft</td>
<td>Variants of certain polymorphisms of this gene (5-HTTLPR, i.e. serotonin transporter gene linked polymorphic region) result in a ‘long’ and ‘short’ allele. Presence of the short allele is a risk factor for MDD. The rs25531 SNP in the promoter region, in certain combinations with the ‘L’ or ‘S’ alleles, may affect antidepressant response. May also mediate antidepressant response in psychotic depression</td>
</tr>
<tr>
<td>Paper(s)</td>
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<tr>
<td>O’Leary et al. (2013)</td>
<td>HTR1A</td>
<td>5q</td>
<td>rs6925</td>
<td>Encodes 5HT₁₄ receptors throughout the brain and CNS</td>
<td>Polymorphisms in this gene have been shown to increase clinical response to antidepressants</td>
</tr>
<tr>
<td>O’Leary et al. (2013)</td>
<td>SLC6A2</td>
<td>16q12.2</td>
<td>rs5569, rs36029, rs1532701</td>
<td>Noradrenaline transporter, removes noradrenaline from the synaptic cleft</td>
<td>Various SNPs are associated with response to tricyclic antidepressants, NRIs and milnacipran (but not SSRIs)</td>
</tr>
<tr>
<td>O’Leary et al. (2013), Adkins et al. (2012)</td>
<td>DAT1 (SLC6A3)</td>
<td>5p15.3</td>
<td>na</td>
<td>Dopamine transporter, removes dopamine from synaptic cleft—primary target of the antidepressant bupropion</td>
<td>Possible association with antidepressant response, association remains unclear</td>
</tr>
<tr>
<td>O’Leary et al. (2013)</td>
<td>COMT</td>
<td>22q11.21</td>
<td>rs4680, rs2075507, rs165599, (rs165599–rs165774–rs174696)</td>
<td>Catechol-O-methyltransferase, an enzyme related to catabolism of noradrenaline and dopamine</td>
<td>Certain polymorphisms and haplotypes are associated with better response to antidepressant drugs</td>
</tr>
<tr>
<td>O’Leary et al. (2013), Adkins et al. (2012), Domschke et al. (2013)</td>
<td>MAOA</td>
<td>Xp11.3</td>
<td>rs6326</td>
<td>Monoamine oxidase A is an enzyme that metabolizes serotonin, noradrenaline, and dopamine</td>
<td>‘Short’ alleles may be related to enhanced antidepressant response. Also, increased risk of psychotic symptoms in depression</td>
</tr>
<tr>
<td>O’Leary et al. (2013)</td>
<td>SLC18A2</td>
<td>10q25</td>
<td>na</td>
<td>Encodes a membrane protein that is important for release of monoamine neurotransmitters from the presynaptic terminal</td>
<td>Possibly implicated in antidepressant response; has yet to be investigated extensively</td>
</tr>
<tr>
<td>O’Leary et al. (2013), Domschke, et al. (2013), Cattaneo et al. (2013)</td>
<td>BDNF</td>
<td>11p13</td>
<td>Nucleotide position 196, ‘Val66met’</td>
<td>Brain derived neurotrophic factor; supports survival of neurons in the brain, affecting neural plasticity</td>
<td>Certain polymorphisms associated with smaller hippocampal volume, and impairments in hippocampal-driven cognition. ‘Met’ allele carriers have improved response to certain antidepressants (e.g., escitalopram) May have an effect on citalopram treatment</td>
</tr>
<tr>
<td>O’Leary et al. (2013)</td>
<td>GRIK4</td>
<td>11q</td>
<td>rs1954787</td>
<td>Encodes a protein in the glutamate neurotransmitter family</td>
<td>Associated with clinical response to antidepressants</td>
</tr>
<tr>
<td>O’Leary et al. (2013)</td>
<td>TREK1 (aka KCNK2)</td>
<td>1q41</td>
<td>na</td>
<td>Neural potassium channel (inhibited by SSRI’s)</td>
<td>Downregulated in antidepressant nonresponders</td>
</tr>
<tr>
<td>Mamdani et al. (2014)</td>
<td>SMAD7</td>
<td>18q21.1</td>
<td>na</td>
<td>Encodes SMA-related and MAD-related protein</td>
<td>Downregulated in antidepressant nonresponders</td>
</tr>
<tr>
<td>Mamdani et al. (2014)</td>
<td>SIGLECP3</td>
<td>19q13.3</td>
<td>na</td>
<td>Sialic acid-binding immunoglobulin-like lectin, pseudogene 3</td>
<td></td>
</tr>
<tr>
<td>Zajkowska et al. (2014)</td>
<td>CNR1</td>
<td>6q15</td>
<td>rs1049353, rs806371</td>
<td>Encode for proteins that lead to formation of endocannabinoid receptors</td>
<td>Certain variants associated with lower susceptibility to depression. Other polymorphisms of these genes are associated with reduced treatment response</td>
</tr>
<tr>
<td>Zajkowska et al. (2014)</td>
<td>CNR2</td>
<td>1p</td>
<td>Q63R, rs2501431</td>
<td>Encode for proteins that lead to formation of endocannabinoid receptors</td>
<td>Certain variants associated with increased severity of depression after 12 weeks of antidepressant treatment</td>
</tr>
<tr>
<td>Zajkowska et al. (2014)</td>
<td>IL-1B</td>
<td>2q</td>
<td>rs16944, rs1143627</td>
<td>Encodes a cytokine protein which is essential to the immune system (specifically, inflammatory response)</td>
<td>Certain polymorphisms of rs16944 are associated with delayed onset of depression in geriatric samples, and certain combinations of polymorphisms on both SNPs listed are linked to recurrent MDD Individuals with a certain allele at this SNP are at increased risk of depression following interferon treatment for Hepatitis C</td>
</tr>
<tr>
<td>Zajkowska et al. (2014)</td>
<td>COX-2</td>
<td>1q</td>
<td>rs4648308</td>
<td>Related to immune system function and metabolism of endocannabinoids</td>
<td></td>
</tr>
</tbody>
</table>
the rs806368 polymorphism of the CNR1 gene predicted citalopram response, with G carrier men exhibiting greater treatment response than TT homozygous men or women. Adkins et al. [12] examined five monoamine candidate genes and found that carriers of the dopamine D4 5-repeat allele exhibited increasing depression during the transition to adulthood, whereas male carriers of the MAOA.3.5 repeat allele exhibited a similar rise in late adolescence. In a study of 243 Han Chinese men and women with MDD, Yeh et al. [13] found that variations in the norepinephrine transporter gene SL6A2 were associated with remission of depression after venlafaxine treatment. In a review of pharmacogenetic and molecular genetic studies, Domschke found that the heritability of psychotic depressive phenotypes was 39%, and that psychotic depression shared several potential chromosomal loci with schizophrenia, schizoaffective disorder, and bipolar disorder [14]. In addition, Domschke found that variants of several genes possibly conferred an increased risk for psychotic symptoms, including BDNF, DBH, DYNBP1, DRD2, DRD4, GSK-3beta, and MAO-A. Thus, future pharmacogenetic work may facilitate the development of individually tailored treatments for psychotic phenotypes based on individual genotypes.

Mamdani et al. [15] examined genetic predictors of citalopram response. They identified SMAD7 and SIGLEC3 as two candidate genes. These genes were the most differentially expressed and significantly downregulated in responders to treatment. Menke [16] found that the most promising candidate genes for depression treatment response are those related to the hypothalamic–pituitary–adrenal (HPA) axis, inflammation, and neuroplasticity; however, another study looking to identify single nucleotide polymorphisms (SNPs)
predictive of antidepressant response found that looking at SNPs related to the HPA axis, endocannabinoid, and immune systems together predicted antidepressant response better than looking at these polymorphisms in isolation [17]. In a GWA study in a sample of over 10,000 individuals, Wray et al. [10] failed to detect main effects for any SNP on depression. These authors estimated that samples 1.8–2.4 times greater are required to sufficiently power genetic association studies of MDD. In addition, Preskorn et al. [18] warn that personalized medicine based solely on genetics may be misleading, given differences between ‘predictor genes’ and ‘target genes’ for antidepressive medications. That is, the biomolecules affected by pharmacological treatment (thereby improving symptoms) can be unrelated to the genes that predict individual response to treatment [19*].

**Therapygenetics**

Targeted interventions based on prescriptive genetics are not limited to pharmacotherapy. Researchers have recently begun to uncover genetic profiles that may predict preferential fit with psychosocial interventions. Perhaps the most promising therapygenetic research to date is Eley et al.’s [20*] finding that children with a short–short genotype for the *SHTT1PR* serotonin transporter gene were more probably to benefit from CBT. Still, Eley [21**] cautions that although therapygenetics offers an encouraging potential benefit, its utility remains limited due to small effect sizes and a lack of replication. Bockting et al. [22*] were unable to replicate the preferential role of *SHTT1PR* in CBT. However, these authors examined the gene by treatment effects on recurrence in remitted adults with depression; future research should examine whether population, diagnosis, or stage of care accounts for the lack of replication. Eley [21**] has proposed a move away from candidate-gene studies to GWA studies to increase power (preferably with large sample sizes), and Lester and Eley [23*] have suggested developing prediction algorithms based on machine learning and the aggregation of multiple genes and polymorphisms.

Finally, the Sequenced Treatment Alternatives to Relieve Depression (STAR*D [24*]) study examined the relationship between ancestral background and outcome after depression treatment in a large cohort of 1892 individuals. Robust correlations between ancestry and both drug efficacy and side effects were observed in 89 different treatment-outcome combinations. These data support the notion that heritable factors (indexed by ancestry) influence side effects as well as outcome of depression treatment.

**Other biological approaches**

Transcranial magnetic stimulation (TMS), the stimulation of regions of the brain via an electromagnetic coil, is an FDA-approved intervention for MDD. Arns et al. were able to reliably identify non-responders to TMS treatment with low false-positive rates [25]. Non-responders tended to exhibit, first, increased pre-fronto-central theta electroencephalography (EEG) power; second, a slower anterior individual alpha peak frequency; third, a larger P300 amplitude; and fourth decreased pre-frontal delta and beta concordance. Fox et al. [26*] demonstrated that individual differences in dorsolateral prefrontal cortex connectivity, as revealed through functional magnetic resonance imaging (fMRI), could be used to individually tailor TMS treatment of depression via the personalized targeting of focal TMS. Finally, Takizawa et al. [27] found that near-infrared spectroscopy could be used to accurately distinguish individuals with MDD from other patient populations with depressive symptoms and may be an important tool for differential diagnosis and personalized care.

**Psychosocial factors and patient characteristics**

In addition to promising biological and genetic approaches, researchers have explored patient characteristics and patient-related psychosocial factors that are predictive of treatment outcome. Hill et al. [28*] have argued that current statistical measurement of change in psychotherapy is too coarse to detect individual complexity and requires augmentation with qualitative and individualized approaches. To this end, Trujols et al. [29*] have proposed the Individual Burden of Illness Index for Depression as a personalized metric for severity and recovery, and Lindhiem et al. [30*] have developed the probability of treatment benefit chart, a probabilistic, individualized metric for determining the chances a given treatment will benefit an individual with various baseline characteristics.

Huang et al. [31] analyzed the electronic health records of 40,651 patients via Least Absolute Shrinkage and Selection Operator logistic regression models. These authors found that they were able to predict future diagnosis of depression as much as a year in advance, with an area under the receiver operating characteristic curve (AUC) of 0.70–0.80. In addition, they were able to differentiate minimal/mild depression from severe depression with an AUC of 0.72. In turn, baseline depression severity was the strongest predictor of treatment response for both pharmacotherapy and psychotherapy – with higher levels of depression predicting poorer outcome in both cases.

DeRubeis et al. [32**] recently introduced the Personalized Advantage Index (PAI) to facilitate optimal selection of treatment plans by five variables (marital status, employment, life events, personality disorder, prior medication trials). Participants were assigned to their ‘optimal’ or ‘non-optimal’ treatment based on PAI scores; those assigned to ‘optimal’ treatment had significantly better treatment outcomes suggesting that this index is useful in guiding treatment selection. Although applied specifically to a pharmacologic versus psychotherapeutic choice,
this method can be applied to any two therapies with existing archival data.

Model-based and statistical methods
Traditionally, researchers have examined ‘what works for whom’ [33] via moderator analyses. However, these efforts have been largely unsuccessful, suffering from poor replication and statistical bias due a lack of random assignment. Wallace et al. [34] recently proposed a novel approach for detecting and interpreting moderator effects via the combination of multiple individual moderators. In a sample of 291 depressed adults, they demonstrated that the combined moderator provided a disordinal (i.e. crossover) effect whereby the preferential benefit of medication was found below the cross point and psychotherapy above the cross point.

Other recent statistical innovations include latent class analysis (LCA) and growth mixture modeling (GMM), which are able to isolate clusters (classes) of responders in psychotherapy outcome data [35–37], with the assumption that understanding the predictors of class membership can generate insight into optimal interventions. In one study, GMM was used to demonstrate that CBT was superior to medication in severely depressed young women at one-year follow-up, with no difference between the interventions at one year in those with moderate depression [38]. Another study found no relationship between intervention modality and treatment response, but demonstrated that non-responder class membership was predicted by coping strategies, emotional lability, and introversion [39].

Two studies have recently examined the latent class structures of interpersonal profiles in MDD. Grosse Holtforth et al. [40] used LCA to examine the distribution of interpersonal circumplex structures in 361 depressed patients and 959 patients with other primary diagnoses. These authors found eight distinct interpersonal classes, with a significantly greater distribution of submissive personality types within the depressed patients. Moreover, class membership was significantly related to baseline severity, with highly introverted individuals exhibiting the most severe depression. Cain et al. [41] conducted an LCA of 312 depressed patients and returned six interpersonal classes — extraverted, dominant, arrogant, cold, submissive, and unassuming. Submissive personality predicted greater chronicity and poorer functioning, indicating a possible need for more intensive or specialized care in these individuals.

Patient preference
Perhaps the most obvious and direct way to personalize treatment is to confer directly with depressed individuals in order to tailor interventions to their preferences. Wittink et al. [42] recently provided a method for determining ‘values markers,’ profiles of patient values and perceptions of what needs to change in depression treatment. LCA of these makers yielded three preference profiles: a pro-counseling/anti-medication profile, a medical setting preference with an aversion to powerful medications, and a preference for medication over counseling. Most participants were classified in ‘profile 1’ in the context of severe depression, and participants generally preferred mental health treatment settings over primary care or spiritual settings. Gaudiano et al. [43] found that men and women may have different beliefs about the cause of their depression, and differing views on the acceptability of treatment regimens. These authors examined the perceived causes of depression and acceptability of medication in 52 psychiatric inpatients and found that women were more likely to make biological causal attributions, and that men who made such attributions were less willing to undergo pharmacologic treatment.

Future directions
Bellon and colleagues have developed the predictD algorithm for determining the presence, level, and risk of onset of MDD for primary care intervention [44]. These investigators are currently conducting a randomized controlled trial of predictD versus usual care, with preliminary results suggesting that patients are comfortable learning about their personal risk of depression [45]. Saveanu and colleagues recently reported initial outcomes from the International Study to Predict Optimized Treatment in Depression (iSPOT-D), an RCT examining escitalopram, sertraline, and venlafaxine-extended release in 1008 treatment-seeking outpatients [46]. Having demonstrated equivalent results across the three treatments, these authors intend to identify potential neurobiological and genetic predictors of optimal treatment.

Finally, our group is currently conducting a proof-of-concept trial based on recent work by the first author [47]. Individuals with MDD and/or generalized anxiety disorder complete brief, phone-based surveys related to the clinical criteria for both disorders, four times per day for 30 days. These data are analyzed to distill the core, latent factors for each individual and the dynamic, predictive relationships among symptoms moment-to-moment. The results of these analyses are then used to make prescriptive decisions about the construction and implementation of modular therapies on a person-by-person basis.

References and recommended reading
Papers of particular interest, published within the period of review, have been highlighted as:

- of special interest
- of outstanding interest


2. Hasin DS, Goodwin RD, Stinson FS, Grant BF: Epidemiology of major depressive disorder: results from the national


This study found that examining SNPs related to the HPA axis, endocannabinoid, and immune systems in combination predicted antidepressant response better than looking at these polymorphisms by themselves. This could provide more insight into the types of genes we can use to predict antidepressant response. In addition, depression treatment response may be influenced by multiple genes or systems of genes in concert with one another.


Preskorn et al. warn that personalized medicine based solely on genetics can be potentially misleading. While the idea that treatment for depression could be signed solely based on genotype is exciting, it may be important to consider a person’s current functioning (i.e. their phenotype). On the basis of one’s genotype, it should be possible to detect how drugs would be metabolized by CYP2D6 isoenzymes. However, certain drugs given for depression can change the phenotype (changing how the drugs are metabolized) without changing the genotype. This highlights the necessity to consider patients’ environments in addition to their genetic profile, as sole focus on genotype may cause important predictors of treatment response to be missed.
This research explored an individualized targeting approach for TMS based on functional connectivity in the brain. Fox et al. demonstrated that individual differences in connectivity (specifically to the dorsolateral prefrontal cortex, which is targeted in TMS treatment) are profound, and are reproducible across sessions. They proposed that, in this way, functional connectivity analyses can be used to personalize targeting of DLPPC TMS, and this approach may be more effective than previous targeting methods based on group-averaged connectivity.


These authors argue that current statistical measurement does not allow researchers to capture nuanced, idiographic changes throughout the process of therapy. Hill et al. recommend that researchers include personalized and qualitative approaches to assess psychotherapy outcome. Individualized studies could include multiple measurements within an individual throughout the course of psychotherapy in order to detect person-specific differences in the trajectory from baseline to post-treatment. This may be a useful tool for distilling what aspects of psychotherapy are effective for different types of participants.


This article reports the use of the ‘Individual Burden Index for Depression’, which was developed using patient input and self-report, to promote the accurate metric of recovery compared to solely clinician’s observations/report. A patient-centered metric of treatment outcome is useful in assessing patient perceptions of recovery. Clinicians and clients may have differing definitions of progress throughout therapy, so it will probably be helpful to capture more detail about clients’ own perception of treatment gains.


This study employed an approach based on the probability of treatment benefit in determining what type of intervention would most benefit children and adolescents. On the basis of individual patient characteristics, projections for the likelihoods of improvement from various interventions were generated. These projections were individual-specific and designed to aid caregivers in selecting an intervention. Offering patients an individually tailored map of information provides a way for patients to make more informed, evidence-based decisions. Such an approach may facilitate therapeutic alliance, perceptions of effectiveness, and potentially treatment outcome.


DeRubies et al. introduce the ‘PAI’ to aid in the selection of individual treatment plans via five variables (malaria status, employment, life events, personality disorder, and prior medication trials). To test this, participants were assigned to their ‘optimal’ or ‘non-optimal’ treatment based on PAI scores; those assigned to ‘optimal’ treatment had significantly better treatment outcomes suggesting that this index is useful in guiding treatment selection.


This study identified latent classes of depression response in low-income minority women. Two latent trajectory classes were returned: first, severe baseline depression and second, moderate baseline depression and anxiety. Women in the first category had exhibited no difference between CBT and medication response at six months but CBT showed superior treatment gains at one year follow-up. For women in the second category, medication was superior at six months, but no differences were observed after one year. This type of approach may be useful for making predictions about who will respond to certain interventions and the trajectory of response during and after treatment. Moreover, this research emphasizes the importance of diversity, which may become increasingly important as the field moves toward personalized treatment approaches. It is possible that we could leverage strategies for tailoring treatment to create more accessible, culturally relevant interventions for underserved populations.


This article describes an RCT to test the ‘predict-D’ algorithm. This algorithm incorporates individual demographic information, SF-12 scores, and other known risk factors for depression to quantify an individual’s risk of depression. This intervention will be implemented by general-practice physicians to identify and prophylactically treat those at risk of developing a MDD diagnosis. This type of preventive treatment could be especially useful from a public-health perspective, by identifying those at risk in an individual-specific way we can hopefully reduce the burden of depression while also using resources (e.g. clinicians’ time) more efficiently.


This large international trial investigated individual predictors of response to three common antidepressant medications. Treatment outcome did not differ across the 1008 outpatients with depression who were randomly assigned to one of three antidepressants (two such as baseline anxiety severity were predictive of treatment response. Future research from this group will continue to delve into the individual factors associated with non-response.