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Neural response to evaluating depression predicts perceivers' mental health treatment recommendations

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Abstract

Nonstigmatized perceivers' initial evaluations of stigmatized individuals have profound consequences for the well-being of those stigmatized individuals. However, the mechanism by which this occurs remains underexplored. Specifically, what beliefs about the stigmatized condition (stigma-related beliefs) shape how nonstigmatized perceivers evaluate and behave toward stigmatized individuals? We examined these questions with respect to depression-related stigmatization because depression is highly stigmatized and nondepressed individuals' behavior (e.g., willingness to recommend treatment) directly relates to removing stigma and increasing well-being. In Study 1, we identified common stigma-related beliefs associated with depression (e.g., not a serious illness, controllable, threatening), and found that only perceptions that depression is a serious condition predicted nondepressed perceivers' willingness to recommend mental health treatment. Moreover, perceivers' beliefs that depression is a distressing condition mediated the relationship between perceived seriousness and treatment recommendations (Study 1). In Study 2, we used fMRI to disentangle the potential processes connecting distress to nondepressed perceivers' self-reported treatment intentions. Heightened activity in the dorsomedial prefrontal cortex (dmPFC)—a region widely implicated in evaluating others—and the ventrolateral prefrontal cortex (vlPFC)—a region widely implicated in regulating negative emotions—emerged when nondepressed perceivers evaluated individuals who were ostensibly depressed. Beliefs that depression is a distressing condition mediated the relationship between dmPFC (but not vlPFC) activity and nondepressed individuals' self-reported treatment recommendations.

Keywords

Stigma; Dorsomedial prefrontal cortex; fMRI; Depression

In everyday life, we constantly evaluate the people we encounter, often without conscious awareness (Bargh & Pietromonaco, 1982; Uleman, Newman, & Moskowitz, 1996). Perceivers' initial evaluations of others predict their subsequent behavior toward their targets (e.g., Ambady & Rosenthal, 1992) and powerfully impact their targets' well-being (Brewer,

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1988; Fiske & Neuberg, 1990). The dorsomedial prefrontal cortex [dmPFC] has been widely implicated in evaluating others (for meta-analyses and reviews, see Denny, Kober, Wager, & Ochsner, 2012; Mitchell, 2009; Van Overwalle, 2009). However, the extent to which activation in the dmPFC and related regions (e.g., ventrolateral prefrontal cortex, temporo-parietal junction, amygdala, and posterior cingulate cortex; Cloutier, Gabrieli, O'Young, & Ambady, 2011; Mende-Siedlecki, Cai, & Todorov, 2012; Schiller, Freeman, Mitchell, Uleman, & Phelps, 2009) predict behavior toward stigmatized individuals outside of the scanner remains largely underexplored (but see Richeson et al., 2003).

Stigma, which refers to any attribute that reduces someone “from a whole and usual person to a tainted, discounted one” (Goffman, 1963:3), has highly pernicious outcomes for its targets (Major & O'Brien, 2005). Social stigma is detected rapidly (Krendl, Zucker, & Kensinger, 2016). Moreover, when nonstigmatized perceivers evaluate highly stigmatized individuals (e.g., homeless individuals), they engage disparate patterns of neural activation (e.g., reduced dmPFC activation) than when they evaluate other stigmatized individuals or nonstigmatized controls (e.g., Harris & Fiske, 2006; Krendl, Macrae, Kelley, Fugelsang, & Heatherton, 2006). Because the dmPFC plays a central role in evaluating others (Denny et al., 2012), reduced activation in this region for some stigmatized targets may shed light on why these groups are dehumanized (e.g., Fiske, Cuddy, Glick, & Xu, 2002).

However, it remains largely unknown how nonstigmatized perceivers' initial evaluations of stigmatized individuals might affect behavior toward those individuals. This question is particularly relevant for mental health conditions such as depression. Mental illness is one of the most stigmatized conditions a person can have (e.g., Hinshaw, 2006) and is associated with robust and pervasive bias (e.g., for review, see Corrigan, 2004). Depression is the most common mental illness in the U.S., affecting nearly 15 million Americans each year (National Institute of Mental Health, 2012). However, as many as two thirds of people suffering from depression do not seek treatment (National Alliance on Mental Illness, 2001), and concerns with being stigmatized have been widely cited as one of the most prominent reasons why (for review, see Corrigan, 2004). Untreated depression is the leading cause of disability in the U.S. (Greenberg, et al., 2003) and the primary cause of suicide, which is the 10th leading cause of death in the U.S. (Centers for Disease Control and Prevention, 2013). Ironically, treatment directly relates to removing these individuals' stigma and increasing their well-being (for review, see Corrigan, 2004).

Although some of the causes and consequences of mental health stigma have been characterized (e.g., Link & Phelan, 2006; Pescosolido, Martin, Lang, & Olafsdottir, 2008), *how* depression-related stigma reduces treatment recommendations more broadly remains unclear. One possibility is that depression-related stigma may affect perceivers' treatment recommendations by activating common beliefs about the stigmatized condition, including the extent to which it is perceived to be controllable, dangerous, not serious, or unfamiliar (Deaux, Reid, Mizrahi, & Ethier, 1995; Fiske et al., 2002; Goffman, 1963; Major & O'Brien, 2005). These beliefs may then generalize to beliefs about the affective impact of the condition (e.g., it is distressing, it is pitiable) (e.g., Batson, Fultz, & Schoenrade, 1987; Leventhal et al., 1992). For instance, if perceivers believe that depression is a serious

condition, they may deem the condition to be more distressing (e.g., Leventhal et al., 1992) and thus be more willing to recommend mental treatment.

Because both depressed and nondepressed individuals do not differ in their levels of explicit or implicit mental health stigma (Teachman, Wilson, & Komarovskaya, 2006), it is likely that these stigmas stem from negative societal beliefs about depression. Thus, understanding how nondepressed perceivers' stigma toward depression affects their willingness to recommend treatment is an important first step in developing interventions that are effective in reducing stigma and promoting treatment. If, as predicted, stigma influences perceivers' beliefs about the affective impact of depression, this could reduce nondepressed perceivers' willingness to recommend mental health treatment either by affecting how they initially evaluate depressed individuals (e.g., Batson et al., 1987; Harris & Fiske, 2006) or by decreasing the regulatory effort they engage to override their negative bias (e.g., Devine, 1989). Simply put, if either perceivers' initial evaluations or regulatory effort predict their treatment recommendations, their beliefs about the affective impact of depression (e.g., how distressing it is) may mediate that relationship.

A neuroimaging approach may be uniquely beneficial in disentangling these disparate mechanisms because the neural correlates underlying evaluating others (e.g., Denny et al., 2012; Mitchell, 2009; Van Overwalle, 2009) and regulating negative emotions (Ochsner, Silvers, & Buhle, 2012) have been well characterized. The present work is the first to examine the potential neurobiological mechanism by which neural activity while evaluating stigmatized (e.g., depressed) individuals generalizes toward endorsing treatment. The current work is an important first step toward developing interventions that might reduce the stigma associated with mental health treatment. For instance, if reduced regulatory effort in response to evaluating depressed individuals predicts nondepressed perceivers' reduced willingness to recommend mental health treatment, it would suggest that interventions that promote regulatory effort might be the most effective in reducing the stigma associated with seeking mental health treatment.

In Study 1, we sought to determine how perceivers' stigma-related beliefs about depression influenced their willingness to recommend treatment (which is unknown). We predicted that the stigma-related beliefs that affected perceivers' treatment recommendations would be mediated by their related beliefs about the affective impact of depression. Study 2 then used fMRI to elucidate a potential neural mechanism by which this may occur. We anticipated that nondepressed perceivers' initial evaluations of depressed individuals or their regulatory effort during those evaluations would predict their willingness to recommend mental health treatment, but that this effect would be mediated by their beliefs about the affective impact of depression. Based on the literature, we hypothesized that this might happen in one of two ways. First, perceivers who believe that depression is a distressing condition may engage more dorsomedial prefrontal cortex (dmPFC) activity when they evaluate depressed individuals (suggesting stronger recruitment of impression formation processes). The extent of dmPFC engagement may then increase their willingness to recommend treatment. Second, perceivers who believe that depression is a distressing condition may have higher activation in neural regions associated with bias regulation (e.g., ventrolateral prefrontal

cortex) when they evaluate depressed individuals. The extent of this engagement may, in turn, also increase their willingness to recommend treatment.

Study 1

A wide body of research has shown that the extent to which people recommend societal beliefs about a stigmatized condition, including the extent to which it is perceived to be controllable, dangerous, not serious, or unfamiliar (Deaux et al., 1995; Fiske et al., 2002; Goffman, 1963; Major & O'Brien, 2005) influences their behaviors toward stigmatized individuals. Perceivers' stigma-related beliefs might then influence their beliefs about the affective impact of the stigmatized condition (e.g., Fiske et al., 2002). For instance, prior work suggests that recommending treatment for others requires perceiving the to-be-treated illness as being serious (e.g., Janz & Becker, 1984), and believing that having the condition would be distressing (for review, see Leventhal et al., 1992). We thus predicted that perceivers' stigma-related beliefs toward depression (e.g., that depression is a serious condition) would predict their willingness to recommend treatment for depressed individuals, but that this relationship would be mediated by their beliefs about the affective impact of depression (e.g., how distressing they perceived having depression to be; how much sympathy they have for individuals suffering from depression).

Three important considerations might also impact perceivers' treatment recommendations: (1) individual differences in beliefs about seeking treatment more generally; (2) depression-related stigmatization (which has been widely shown to disrupt treatment seeking; Corrigan, 2004); and (3) personal experiences with depression (either by oneself or a close friend). Regarding individual differences in beliefs about seeking treatment, some nonstigmatized perceivers might be more willing to seek treatment for any illness, and/or more likely to perceive any condition as having a negative affective impact on its bearer. Our central interest in the current study was to identify the stigma-related beliefs that predicted nondepressed perceivers' willingness to recommend treatment for depression above and beyond individual differences in perceivers' general beliefs about all illnesses. We therefore also measured treatment recommendations and beliefs for a nonstigmatized illness: migraines. With respect to measuring personal experiences with depression, prior work suggests that perceivers' mental health stigma does not differ as a function of whether or not they personally know someone with a mental health problem (e.g., a family member; Crisp, Gelder, Rix, Meltzer & Rowlands, 2000; Moses, 2010). However, it is less well understood whether familiarity affects mental health treatment recommendations. We therefore included this item as a conceptual replication and extension of prior work.

Method

Participants—Seventy Indiana University undergraduate students (18–30 years of age, 48 female) participated. Of the 70 participants, 55 identified as Caucasian (78.6%), 7 (10%) as Black, 3 (4%) as Asian, 4 (5.7%) as more than one race, and 1 did not provide race information. A priori power analyses conducted in G*Power (Faul, Erdfelder, Lang, & Buchner, 2007) using a medium effect size ($f^2 = .35$), $\alpha = .05$, and power = .95, indicated 67 participants would detect effects.

Materials—We measured treatment recommendations, sympathy, and distress using two novel vignettes describing two different individuals. One vignette described an individual suffering from symptoms commonly associated with depression, while the other described an individual suffering from migraines (which served as the control condition). Pilot testing with a separate group of undergraduates at Indiana University confirmed that migraines and depression were perceived as similarly familiar, treatable, and emotionally arousing (see Supplemental Materials for validation of these vignettes). The vignettes were written in similar styles and length, and the gender of the described individual always matched participant gender. Participants viewed the two vignettes in pseudorandom order, and were asked after reading each. “How distressing do you believe the person’s condition is? How sympathetic are you to the person described?,” and “If you were friends with this person, how likely would you be to recommend that s/he seek professional treatment?” For all items, the scale ranged from 1 (*not at all*) to 7 (*very much*).

Participants then completed a series of filler tasks. After, we measured their stigma-related beliefs about depression using the following ratings (presented in pseudorandom order): “How responsible do you think someone with depression/migraines is for their condition?” (responsibility); “How likely do you think it is that someone suffering from depression/migraines can change their condition?” (changeability); “How serious do you think depression/migraines is?” (seriousness of disorder); “How much of a threat do you think people with depression/migraines pose to themselves or others?” (perceived threat). All ratings were made on a 1 (*not at all*) to 7 (*very much*) scale and were self-paced. Prior work has identified these beliefs as the primary dimensions by which stigmatized conditions are evaluated (e.g., Deaux et al., 1995; Feldman & Crandall, 2007; Goffman, 1963).

We measured participants’ personal familiarity with depression by asking them to indicate whether they or someone they knew had ever suffered from depression or migraines (via yes/no response), and, if so, how well. They also completed the Internalized Stigmatization Scale (ISS; Ritsher, Otilingam, & Grajales, 2003), which measures mental health stigmatization. We modified the ISS from its original version to refer specifically to depression instead of mental illness. The interitem reliability was acceptable (Cronbach’s $\alpha = .72$).

Results

Comparing ratings for depression and migraines—Consistent with our pilot testing for the vignettes (see Supplemental Materials), participants did not differ in their willingness to recommend treatment for depression ($M_{\text{Depression}} = 6.07$, $SD = 1.29$) and migraines ($M_{\text{Migraines}} = 6.21$, $SD = 1.41$; $t < 1$). They also did not differ in their perceptions that the two conditions were distressing ($M_{\text{Depression}} = 5.46$, $SD = 1.26$; $M_{\text{Migraines}} = 5.57$, $SD = 1.03$) or elicited sympathy ($M_{\text{Depression}} = 5.54$, $SD = 1.45$; $M_{\text{Migraines}} = 5.69$, $SD = 1.22$), both t s < 1 . Regarding their stigma-related beliefs toward the two illnesses, perceivers did not differ in their perceptions regarding controllability of the two illnesses (responsibility: $M_{\text{Depression}} = 2.61$, $SD = 1.61$; $M_{\text{Migraines}} = 2.27$, $SD = 1.60$; changeability: $M_{\text{Depression}} = 2.73$, $SD = 1.31$; $M_{\text{Migraines}} = 2.70$, $SD = 1.41$), both t s < 1.64 , p s $> .10$. However, they rated depression as being more serious than migraines ($M_{\text{Depression}} = 6.29$, $SD = 1.00$; $M_{\text{Migraines}}$

= 5.37, $SD = 1.33$); $t(69) = 5.63, p < .001$, as well as more threatening ($M_{\text{Depression}} = 4.71, SD = 1.63$; $M_{\text{Migraines}} = 2.41, SD = 1.32$); $t(69) = 11.52, p < .001$.

A closer examination of the ratings for the two illnesses revealed that they were all highly correlated with one another (all $r_s > .27, p_s < .05$). For instance, perceptions that migraines is a serious disorder was correlated with perceptions that depression is a serious disorder, $r(68) = .35, p = .003$. The same pattern emerged for perceptions that migraines and depression are threatening, $r(68) = .38, p < .001$, and distressing, $r(68) = .53, p < .001$. (See Supplemental Materials for a complete table of the correlations between all of the ratings.) Together, the fact that these ratings were highly correlated suggested that individual differences contributed to perceivers' ratings. That is, the extent to which an individual perceived depression to be a serious illness was likely influenced more generally by how serious the perceiver found any illness to be. To control for individual differences in responding, we therefore created difference scores for each rating (e.g., willingness to recommend treatment for depression—willingness to recommend treatment for migraines). Using these difference scores allowed us to ask the more specific question: why are perceivers' more (or less) likely to recommend treatment for depression than migraines?

Identifying the stigma-related beliefs that predicted mental health treatment recommendation—Using the abovementioned difference scores, we used linear regression to identify stigma-related belief(s) (low perceived seriousness, high responsibility, high changeability, and/or high threat) that predicted their treatment recommendations for depression (vs. migraines) when controlling for participants' familiarity (either themselves or someone they knew) with depression and their mental health stigma beliefs (using ISS). The overall model was significant, $F(6, 68) = 4.49, p = .001$, and accounted for 30% of the overall variance in treatment recommendations.¹ Supporting our hypothesis, perceived seriousness for depression (vs. migraines) was the only significant predictor ($\beta = .40, t = 3.658, p = .001$). None of the other stigma-related beliefs (responsibility, changeability, or threat) predicted treatment recommendations (all $\beta_s < .21, t_s < 1.80, p_s > .08$). See Table 1 for all relevant statistics.

Perceived seriousness mediates relationship between distress and treatment recommendations—We next examined whether perceivers' beliefs that depression is a distressing condition or their sympathy for individuals suffering from depression (vs. migraines) were associated with perceived seriousness. The overall model was significant, $F(2, 68) = 10.32, p < .001$, and accounted for 24% of the overall variance. Distress was the only significant predictor ($\beta = .44, t = 3.68, p < .001$; sympathy: $\beta = .10, t = .81, p = .42$).² Consistent with our hypothesis, mediation analyses using PROCESS with 1,000 bootstrap

¹Participants who did not know anyone with depression (20 out of the 70 participants) were coded as zero for this analysis. However, excluding those 20 participants does not affect the overall model. Indeed, the model was still significant, $F(5, 48) = 6.28, p < .001$, for the 50 participants who knew someone with depression, and accounted for 42.2% of the overall variance. Again, the belief that depression is serious was significant in this model ($\beta = .46, t = 3.84, p < .001$). Familiarity more generally did not predict treatment intentions alone or in the model (all $t_s < 1$). Indeed, the first model in Study 1 remained significant when excluding familiarity and bias (for all 70 participants), $F(4, 69) = 6.29, p < .001$, and accounted for 24% of the overall variance.

²When we ran the regressions from Study 1 with only White participants, the same pattern of results emerged. Specifically, the overall model predicting treatment recommendations from perceivers' stigma-related belief(s) toward depression (vs. migraines) (perceived seriousness, responsibility, changeability, and/or threat) when controlling for participants' familiarity with depression and their mental health stigma was significant, $F(6, 54) = 2.86, p = .028$, and accounted for 24% of the overall variance in treatment recommendations.

samples (Hayes, 2012) showed that although perceptions that depression (vs. migraines) is a serious illness positively predicted treatment recommendations, it acted through perceivers' beliefs that depression (vs. migraines) is a distressing condition, $B = .20$, $SE = .06$, 95% CI [.09, .33]. The effect size of the indirect effect was $R^2 = .17$, $SE = .07$, bootstrap 95% CI [.05, .32]. See Figure 1.³

Discussion

Study 1 showed that perceptions that depression is perceived to be a more distressing condition than migraines contributed to perceivers' greater willingness to recommend treatment for depression (vs. migraines). This effect was not influenced by perceivers' personal (via self or other) familiarity with depression. As predicted, the extent to which perceivers believed that depression was more distressing than migraines mediated the relationship between perceived seriousness and treatment recommendations. Study 2 used neuroimaging to identify the neural processes engaged when nondepressed individuals evaluate depressed individuals. Of interest was whether the neural regions engaged in nondepressed individuals' initial evaluations of depression predicted their behavior (self-reported mental health treatment-seeking intentions).

Study 2

The two goals of Study 2 were to (1) extend prior neuroimaging work on stigma by demonstrating that nondepressed perceivers engaged a unique pattern of neural activity when they evaluated individuals suffering from depression as compared to a nonstigmatized illness (migraines) or healthy controls (Hypothesis 1); and (2) determine whether perceivers' beliefs that depression is a distressing condition mediated a potential relationship between the neural correlates underlying their initial evaluations and subsequent treatment recommendations.

Stigma is detected rapidly (Krendl et al., 2016), and affects the neural mechanisms engaged by nondepressed perceivers during their initial evaluations of stigmatized individuals (e.g., Harris & Fiske, 2006; Krendl et al., 2006; Krendl, Kensinger, & Ambady, 2012; Krendl et al., 2016). We hypothesized that perceivers' initial evaluations of depressed individuals could predict their treatment recommendations in one of two ways. First, perceivers who believe that depression is a distressing condition may engage more dorsomedial prefrontal cortex (dmPFC) activity when they evaluate depressed individuals (suggesting stronger recruitment of impression formation processes; for meta-analyses and reviews, see Denny et al., 2012; Mitchell, 2009; and Van Overwalle, 2009). DmPFC plays a causal role in impression formation (Ferrari et al., 2014; Ferrari, Vecchi, Todorov, & Cattaneo, 2016), and

As with the full sample, only perceived seriousness was significant ($\beta = .424$, $t = 3.31$, $p = .002$). We also found that the overall model with perceived distress and sympathy toward depression as potential predictors for beliefs that depression is a serious illness was significant, $F(2, 54) = 7.18$, $p = .002$, and accounted for 21.6% of the overall variance. As with the full sample, perceived distress was the only significant predictor ($\beta = .42$, $t = 3.12$, $p = .003$; sympathy: $\beta = .11$, $t = .83$, $p = .41$).

³Although our mediation analysis suggests that the relationship between beliefs that depression (vs. migraines) is serious and treatment recommendations for depression (vs. migraines) is mediated by distress, it is also plausible that seriousness mediates the relationship between distress and treatment recommendations. We therefore conducted a second mediation analyses using PROCESS with 1,000 bootstrap samples (Hayes, 2012), in which distress was the mediator. Here we found that although distress in response to depression positively predicted treatment recommendations, it acted through the extent of stigma-related beliefs of depression (vs. migraines) as a serious illness, $B = .14$, $SE = .08$, 95% CI [.03, .34].

is engaged regardless of whether impressions are spontaneous or intentional (Ma, Vandekerckhove, Van Overwalle, Seurinck, & Fias, 2011). Moreover, dmPFC plays a prominent role in forming impressions of dissimilar others (Mitchell, Macrae, & Banaji, 2006) and evaluating stigmatized individuals (Harris & Fiske, 2006). If, as predicted, dmPFC is more active when perceivers evaluate depressed (as compared to nondepressed) individuals, then one possibility is that the extent of their dmPFC engagement may predict their willingness to recommend treatment.

It is also possible that perceivers who believe that depression is a distressing condition may engage more regulatory effort when they evaluate depressed individuals. The ventrolateral prefrontal cortex (vlPFC) has been widely implicated in regulating negative emotional responses (Ochsner et al., 2012), as well as in forming impressions of stigmatized individuals (e.g., Krendl, Kensinger, et al., 2012; Krendl et al., 2016). Moreover, the magnitude of vlPFC activation corresponds with perceivers' implicit bias toward stigmatized individuals (e.g., Krendl, Heatherton, & Kensinger, 2009; Krendl, Kensinger, et al., 2012). For this reason, as well as the fact that explicit bias did not predict treatment recommendations in Study 1, we included a measure of implicit bias in Study 2. If, as predicted, vlPFC is more active when perceivers evaluate depressed (as compared to nondepressed) individuals, then another possibility is that the extent of their vlPFC engagement during their initial evaluations would be associated with their bias and would predict their willingness to recommend treatment.

Despite the fact that early treatment seeking predicts the greatest treatment success (e.g., Altamura et al., 2010), an important obstacle to seeking treatment is one's ability to correctly attribute one's symptoms (e.g., feeling down or lethargic) to depression. Moreover, prior research in clinical populations suggests that individuals' attitudes toward mental health treatment play a central role in predicting their actual help-seeking intentions (e.g., Bayer & Peay, 1997; Mojtabai, Olfson, & Mechanic, 2002). Thus, to better generalize Study 1, Study 2 assessed self-reported intentions to seek mental health treatment in addition to willingness to recommend mental health treatment for others. We predicted that self-reported treatment-seeking intentions would be positively correlated with mental health treatment recommendations for others, and verified this assumption using the same vignettes as described in Study 1. Further, we predicted that participants' belief that depression is a distressing condition (as measured in the vignettes from Study 1) would influence their own self-reported treatment intentions. These were measured in a separate testing session approximately 1 week prior to the fMRI session.

We predicted that evaluating depressed individuals would elicit heightened activation in dmPFC and/or vlPFC (as compared to evaluating individuals with migraines or healthy controls; Hypothesis 1). Moreover, if nondepressed individuals' neural activity when they evaluated depressed individuals related to their own self-reported treatment-seeking intentions, we anticipated that perceivers' belief that depression (vs. migraines) is a distressing condition would mediate the relationship between either dmPFC (which would suggest greater impression formation) or vlPFC (which would suggest regulation) and self-reported treatment-seeking intentions (Hypothesis 2).

Method

Participants—Thirty right-handed White adults with no history of neurological problems (18–29 years of age, 17 female) from Indiana University participated and provided informed consent. This sample size was selected to ensure sufficient power for our analyses (Desmond & Glover, 2002). Participants were screened to ensure that they had not previously, nor were they currently, suffering from depression. Participation was completed over two testing sessions, approximately 1 week apart. The first session was conducted in the laboratory and consisted of a series of behavioral measures described below. A portion of the behavioral data from one participant was lost due to a computer error. The second session was the fMRI study. Participants completed the fMRI study described below and a separate study unrelated to mental health. Study order was counterbalanced, and no order effects were found. Because stigma interacts with attitudes toward treatment seeking differently as a function of perceivers' race (e.g., Brown et al., 2010; Givens, Katz, Bellamy, & Holmes, 2007) and ethnicity (e.g., Georg Hsu et al., 2008; Rao, Feinglass, & Corrigan, 2007), we selected a racially and ethnically homogeneous group for the current study in order to most accurately interpret our results. We chose White participants for two reasons. First, the majority of participants in Study 1 were White (79%). Second, the unrelated study was about race, making White participants the preferred participant population for both.

Procedure

Behavioral testing session: Participants completed an fMRI screening and measures relevant to the present task and others in the laboratory approximately 1 week prior to scanning. In this session, we measured participants' treatment recommendations for others and beliefs that depression is a distressing condition (using the same vignettes from Study 1), their self-reported treatment-seeking intentions, and their implicit bias toward depression (described below). Participants also completed the 22-item short version of the Empathy Quotient to control for individual differences in empathy (Wakabayashi et al., 2006).

Assessing participants' self-reported mental health treatment-seeking intentions: To measure self-reported intentions toward seeking mental health treatment, participants evaluated three statements describing common symptoms of depression and three statements describing common symptoms of migraines (see Appendix B in the Supplemental Materials for items). Critically, the symptoms for each illness became progressively more serious with each statement (low, moderate, severe). For depression, the first two statements included symptoms from the PHQ-2, a two-item measure assessing depression that, combined, has a sensitivity of 83% and specificity of 92% for diagnosing major depression (Kroenke, Spitzer, & Williams, 2003). The third (highest) symptom severity item specifically addressed suicidality. These items had strong reliability (Cronbach's $\alpha = .84$). For migraines, the items were structured to parallel depressive symptoms, and were compiled via Internet search engines identifying the most common symptoms of migraines (e.g., experiencing a dull ache on the side of one's head for a few hours per day for multiple days over the past month, having difficulty concentrating on work). The high-severity symptoms also included experiencing symptoms of nausea and vomiting. These items had acceptable reliability (all Cronbach's $\alpha = .72$). For each question, participants indicated their likelihood of seeking treatment if they experienced a specific set of symptoms.

We measured participants' willingness to seek treatment for both depression and migraines to control for individual differences in treatment seeking in general. For instance, an individual who is reluctant to seek treatment for any illness would likely have lower treatment intentions for both migraines and depression as compared to an individual who is more willing to seek treatment for any illness. We thus calculated disparity scores between willingness to seek treatment for depression as compared to migraines to use in our subsequent analyses.

In addition to controlling for individual differences in treatment seeking, we were interested in identifying the symptom severity level at which participants were most reluctant to seek treatment for depression (relative to migraines). We did this to increase our sensitivity in detecting whether individual differences in neural activity associated with depression predicted behavior (self-reported treatment intentions for depression specifically). We posited that greater ambivalence for seeking treatment for depression (relative to migraines) would be reflected by higher disparity scores and more variability in the disparity scores for that symptom level.

We thus conducted a 2 (illness: migraines or depression) \times 3 (symptom severity: low, moderate, severe) repeated-measures ANOVA on the intentions measures. Results revealed a main effect of illness, $F(1, 28) = 49.63, p < .001, \eta_p^2 = .64$, a main effect of symptom severity, $F(1, 28) = 126.55, p < .001, \eta_p^2 = .82$, and an Illness \times Severity interaction, $F(1, 28) = 11.06, p < .001, \eta_p^2 = .28$. The main effects emerged because participants had higher intentions to seek treatment for migraines as compared to depression, regardless of symptom severity. They also had higher treatment intentions for both illness types as they increased in symptom severity (see Supplemental Materials for all means). The interaction emerged because the disparity between treatment intentions for migraines and depression differed as a function of symptom severity. Specifically, the disparity was lowest for the high-severity condition ($M_{\text{Migraines} - \text{Depression}} = .90, SD = 1.21$), higher for the low-severity condition ($M_{\text{Migraines} - \text{Depression}} = 1.69, SD = 1.44$), and highest for the moderate-severity condition ($M_{\text{Migraines} - \text{Depression}} = 2.07, SD = 1.60$). This resulted in a significant linear effect, $F(2, 56) = 11.06, p < .001, \eta_p^2 = .28$. The disparity between the low-severity and moderate-severity conditions did not differ significantly from one another, $t(28) = 1.52, p = .14$, but both significantly differed from the high-severity condition (both $t_s > 2.80, p_s < .01$). However, of the three symptom severity levels, the moderate-severity condition elicited the most variance in participant responses and also had the highest disparity. Thus, our subsequent analyses used participants' self-reported treatment intentions (depression – migraines) as reported for the moderate-symptom severity level.

Measuring implicit bias: Implicit bias was assessed using the Implicit Association Test (IAT; Greenwald, McGhee, & Schwartz, 1998) that was designed to measure implicit bias toward depression (using the categories depressed/not-depressed, pleasant/unpleasant). Specifically, participants categorized six images of depressed individuals (three male, three female), six images of nondepressed individuals (three male, three female), six pleasant words (e.g., *kindness*), and six unpleasant words (e.g., *jealousy*). Participants completed stereotypically congruent (e.g., a pleasant word paired with a nondepressed individual) and incongruent (e.g., a pleasant word paired with a depressed individual) blocks (order was

counterbalanced across participants). Consistent with recommended scoring procedures (Greenwald, Nosek, & Banaji, 2003), we removed trials with less than 200 ms and over 3,000 ms and then calculated IAT D (which divides the reaction time difference between incongruent and congruent blocks by the standard deviation of all latencies) to measure implicit bias toward depression.

FMRI stimuli and task—In the scanner, participants viewed 120 Caucasian faces with neutral expressions drawn from the PAL database (Minear & Park, 2004). Forty faces were identified as depressed, 40 as migraine afflicted, and 40 as healthy. Faces were equated for attractiveness, distinctiveness, and trustworthiness across conditions (see Cassidy & Gutchess, 2012). We conveyed diagnosis by placing the face on a red, green, or yellow background (see Cloutier et al., 2011, for a similar approach). The color–diagnosis pairing was counterbalanced across participants, as were faces and diagnosis category. To ensure attention to the color–diagnosis pairings, participants reported at three separate time points (after instructions, the first scan, and immediately posttask) which diagnosis was paired with which color. All participants successfully did this at every assessment point.

The task was modeled as an event-related design over one run that lasted 5 minutes and 38 seconds (169 TRs; 1 TR = 2s). Participants viewed each face for 2 seconds and indicated via button press how much they liked the individual pictured on a 4-point scale (1 = *highly dislike*, 4 = *highly like*). We asked participants to indicate how much they would like the targets because prior work has shown that dmPFC is engaged during impression formation regardless of task instructions, but vlPFC is engaged during intentional impression formation (Ma et al., 2011). Our design optimized the likelihood of detecting activity in both regions. Images were randomly presented, with no more than two of the same diagnosis type sequentially. Periods of jitter, in the form of a fixation cross at the center of the display, ranged from 2 to 8 seconds. Participant responses were monitored to ensure attention during the task.

Data acquisition and analysis—Whole-brain imaging was performed on a Siemens 3.0T TIM Trio MRI scanner at the Indiana University Imaging Research Facility in Bloomington, Indiana. Anatomical images were acquired with a high-resolution 3-D magnetization-prepared rapid gradient-echo sequence (224 slices; echo time [TE] = 3.02 ms; repetition time [TR] = 2,200 ms; flip angle = 9°; .8 × .8 × .8-mm voxels). Functional images were collected over one run of 169 time points, using a fast field echo-planar sequence sensitive to blood-oxygen-level-dependent contrast (T2*; 32 slices with 3.5-mm thickness and 3.5-mm skip; TR = 2,000 ms; TE = 30 ms; flip angle = 70°).

Preprocessing and analyses of functional data were conducted in SPM8 (Wellcome Trust Centre for Neuroimaging, London, UK). Images were realigned to correct for motion, normalized to the MNI (Montreal Neurological Institute) template, and smoothed using a 6-mm FWHM isotropic Gaussian kernel. We used custom artifact detection software to detect motion artifact after preprocessing (http://www.nitrc.org/projects/artifact_detect) in individual runs on a participant-by-participant basis. We applied a priori motion criteria that participants be excluded if they moved more than 2 mm during the functional run or that individual volumes be removed (as nuisance regressors) if head motion on that volume

exceeded 1 mm or the overall signal for that time point fell three standard deviations outside the mean global signal for the entire run. None of the participants met either exclusionary criteria, and therefore no participant or volume was removed.

Data were resampled to 3-mm isotropic voxels in a 96×96 matrix. A general linear model incorporating the three image types (faces of ostensibly depressed, migraine-afflicted, or healthy individuals) and covariates of no interest (a session mean, a linear trend, and six movement parameters derived from realignment corrections) computed parameter estimates (β) and t -contrast images (containing weighted parameter estimates) for each comparison at each voxel and for each participant. We conducted a whole-brain ANOVA, with condition (condition: depressed, migraines, healthy) as the independent variable.

Individual differences were examined using region of interest (ROI) analyses based on the results from the whole-brain ANOVA. For all ROI analyses, we averaged the parameter estimates from the 8-mm sphere surrounding the peak coordinate of interest (see fMRI results for specific peaks) using the relevant condition–baseline contrast. For the ANOVA, we used an extent threshold of $p < .001$, with a 10-voxel extent threshold correction (see Lieberman & Cunningham, 2009).

Results

Behavioral results

Recommending treatment and distress for depressed others predict self-reported treatment seeking intentions: As in Study 1, perceivers did not differ in how distressing they found having migraines or depression to be based on the vignettes ($M_{\text{Depression}} = 5.72$, $SD = 1.07$; $M_{\text{Migraines}} = 5.69$, $SD = 1.04$, $t < 1$); how much sympathy they had for individuals with either illness ($M_{\text{Depression}} = 5.83$, $SD = 1.39$; $M_{\text{Migraines}} = 5.83$, $SD = 1.20$, $t < 1$); or their willingness to recommend treatment for either illness ($M_{\text{Depression}} = 6.17$, $SD = .89$; $M_{\text{Migraines}} = 6.45$, $SD = .78$), $t(28) = 1.77$, $p = .09$. Also as in Study 1, perceivers' ratings for migraines and depression were highly correlated with each other—sympathy: $r(29) = .56$, $p < .005$; distress $r(29) = .63$, $p < .001$; treatment recommendation: $r(29) = .50$, $p < .01$.

We used difference scores (depression – migraines) for all reported analyses (see Study 1 for rationale). An important goal of Study 2 was to better generalize treatment recommendations for others to participants' own self-reported treatment intentions because clinical research suggests that attitudes toward mental health treatment play a central role in predicting actual help-seeking intentions (e.g., Bayer and Peay, 1997; Mojtabai et al., 2002). To verify this, we examined whether self-reported treatment seeking intentions (for depression – migraines) and treatment recommendations for others (depression vignettes – migraines vignettes) were related. Self-reported treatment seeking intentions and treatment recommendations for others from the vignettes were positively correlated, $r(29) = .41$, $p = .027$. Moreover, perceptions that depression (vs. migraines) is a distressing condition predicted self-reported treatment-seeking intentions for depression (vs. migraines), $r(29) = .57$, $p = .001$.⁴

Likability ratings during the fMRI task: We conducted a repeated-measures ANOVA to determine whether participants' explicit likeability ratings during the scanning session differed by diagnosis (depressed, migraines, healthy). A marginal effect emerged, $F(1, 29) = 3.112$, $p = .088$, $\eta_p^2 = .097$. Participants had slightly lower liking ratings for depressed and migraine-afflicted individuals ($M_{\text{Depressed}} = 2.419$, $SD = .287$; $M_{\text{Migraine}} = 2.440$, $SD = .310$) versus healthy individuals ($M_{\text{Healthy}} = 2.545$, $SD = .370$). Because these results did not reach traditional levels of significance, they should be cautiously interpreted.

fMRI results

Hypothesis 1: DmPFC and vIPFC are more active when nondepressed participants form impressions of depressed individuals: A whole-brain ANOVA identified neural activity differing by diagnosis (healthy, depression, migraines). The ANOVA revealed main effects in the dmPFC (BA 9: 0, 33, 39), right VLPFC (BA 47: 51, 36, -6), and left superior frontal gyrus (BA 9: -21, 60, 30). As expected, subsequent ROI analyses revealed that activation in these regions was driven by the depression diagnosis condition. Specifically, evaluating depressed (vs. migraine-afflicted or healthy) individuals elicited heightened activation in these regions (see Table 2 and Fig. 2). For t-tests directly comparing each condition, see Table 3.

Hypothesis 2: Distress toward depression mediates the relationship between dmPFC, but not vIPFC, activity and self-reported treatment intentions: We next tested whether distress mediated a relationship between dmPFC or vIPFC activity and perceivers' self-reported mental health treatment-seeking intentions. Here, we used the dmPFC and vIPFC peaks that emerged from the main effect of diagnosis condition in the whole-brain ANOVA (dmPFC: 0, 33, 39), and (vIPFC: 51, 36, -6). Since dmPFC or vIPFC activity could also mediate a relationship between distress and self-reported mental health treatment-seeking intentions, we tested both models using PROCESS in SPSS with 1,000 bootstrap samples (Hayes, 2012). As in Study 1, we used difference scores (depression – migraines) for all analyses. Thus, the difference scores identified patterns of neural activation that may have differed when perceivers evaluated depressed individuals as compared to when they evaluated individuals suffering from migraines.

In our first model, significant indirect effects emerged between dmPFC activation and self-reported intentions to seek treatment. As predicted, although dmPFC response when evaluating depressed individuals positively predicted self-reported treatment intentions (for depression vs. migraines), distress mediated this relationship, $B = .22$, $SE = .16$, 95% CI [.04, .67]. The effect size of the indirect effect was $R^2 = .12$, $SE = .06$, bootstrap 95% CI [.02, .26] (see Fig. 3).⁵

⁴It is worth noting that self-reported treatment intentions for the low symptom severity did not correlate with treatment recommendations, $r(28) = .22$, $p = .25$.

⁵We also conducted the mediation analysis using participants' self-reported intention to seek treatment for the low-symptom severity level. Here, although dmPFC activation positively predicted self-reported treatment intentions, $r(28) = .43$, $p = .021$, distress was not significantly related to treatment intentions for low-symptom severity, $r(28) = .27$, $p = .17$. Finally, we examined whether perceivers' stigma-related beliefs that depression is a serious illness (which was the only belief that predicted their willingness to recommend treatment in Study 1) mediated the relationship between dmPFC activation and self-reported treatment seeking intentions at the moderate symptom severity. The indirect effect in this model was not significant: $B = .003$, $SE = .05$, 95% CI [-0.06, .17]. The effect size of the indirect effect was $R^2 = .002$, $SE = .03$, bootstrap 95% CI [-0.04, .08].

The extent of vIPFC activity in response to evaluating individuals suffering from depression as compared to migraines was positively correlated with dmPFC activity: $r(30) = .61, p < .001$, and marginally correlated with perceivers' implicit bias (IAT D): $r(30) = -.35, p = .060$. However, it was not related to their self-reported treatment intentions: $r(30) = .01, p = .98$. Similarly, the model examining whether perceived distress mediated a potential relationship between vIPFC activation and self-reported treatment intentions was not significant, $B = .37, SE = .35, 95\% \text{ CI} [-.14, 1.23]$. The effect size of the indirect effect was $R^2 = -.02, SE = .05$, bootstrap 95% CI $[-.19, .03]$.

Discussion

Study 2 revealed two key findings. First, perceivers had increased dmPFC and vIPFC activation when evaluating depressed (vs. migraine-afflicted and healthy) individuals (Hypothesis 1). Second, perceivers who had a greater extent of engagement in impression formation processes (dmPFC) when they evaluated individuals suffering from depression (as compared to migraines) had a smaller difference between their self-reported treatment-seeking intentions for depression as compared to migraines. Perceptions that depression is a more distressing condition than migraines mediated the relationship for dmPFC and treatment recommendations (Hypothesis 2). Activity in the vIPFC was not associated with self-reported treatment-seeking intentions, but it was marginally associated with perceivers' implicit bias (with more bias predicting less vIPFC engagement for depression vs. migraines).

General discussion

The present work identified the first potential neurobiological mechanism for how neural activity associated with evaluating depressed individuals predicts nondepressed perceivers' self-reported mental health treatment-seeking intentions. Specifically, dmPFC activity in response to evaluating depressed individuals predicted self-reported treatment-seeking intentions for depression. However, this relationship acted through distress. These findings have direct relevance to advancing our understanding of how stigma-related beliefs about depression impact nondepressed perceivers' willingness to recommend or seek mental health treatment.

Our results suggest that stronger engagement of dmPFC positively predicts perceivers' self-reported treatment-seeking intentions. In order to determine whether the dmPFC peak observed in the current study was a region implicated in evaluating others, we examined a meta-analysis on studies examining the neural correlates underlying judgments about others (vs. self; Denny et al., 2012). We found that the dmPFC activity we observed in the current study is indeed similar to the dmPFC region implicated by the meta-analysis in evaluating others. One potential explanation for this finding is that when perceivers evaluate depressed individuals, the extent to which they engage neural processes associated with evaluating others may be associated either with reduced dehumanization or greater individuation of depressed individuals. For instance, Harris and Fiske (2006) found that nonstigmatized perceivers had reduced activation in the dmPFC when they evaluated highly stigmatized individuals (e.g., homeless individuals), and suggested that this may provide insight into

why highly stigmatized groups are dehumanized (e.g., Fiske et al., 2002). Being humanized has been associated with many interpersonal benefits, such as a heightened moral status (Bastian, Laham, Wilson, Haslam, & Koval, 2011), fairer treatment, and greater empathy (Cehajic, Brown, & Gonzalez, 2009). Dehumanization of outgroup members reverses these effects and is associated with greater aggression (Viki, Osgood, & Phillips, 2013), discrimination (Pereira, Vala, & Leyens, 2009), and harsher punishments (Fincher & Tetlock, 2016) toward dehumanized individuals. DMPFC engagement may therefore be an important link between evaluation and behavior because it may reflect perceivers' increased humanization of depressed individuals and thus greater willingness to recommend treatment for those individuals.

In addition to increased activity in dmPFC, participants also had heightened vIPFC activation when they evaluated depressed individuals. Although vIPFC activity did not predict distress or treatment-seeking intentions for depression versus migraines, it was positively associated with dmPFC activity and had a marginally negative association with implicit bias. One speculative possibility is that this region, which has been widely implicated regulating negative responses (for review, see Amodio, 2014; see also Cassidy, Lee, & Krendl, 2016; Krendl et al., 2012), may play a role in downregulating perceivers' stigma-related bias during initial evaluations. Given that treatment recommendations were not directly predicted by explicit bias in measured Study 1, and stigmatized individuals elicit multiple parallel neural responses during impression formation (e.g., Harris & Fiske, 2006; Krendl et al., 2012; Krendl et al., 2006)—some of which are associated with bias (e.g., Krendl, Kensinger, et al., 2012)—future research should further investigate this question.

Study 1 demonstrated that perceivers' beliefs that depression is a serious illness corresponded with increased beliefs that depression is a distressing condition. Moreover, perceived seriousness mediated the relationship between distress and treatment recommendations. However, Study 2 found that only perceptions that depression is more distressing than migraines (not that it is more serious; see footnote 5) predicted greater dmPFC activity when evaluating depressed versus migraine-afflicted individuals. One possible explanation for this finding is that recommending treatment for depressed (vs. migraine-afflicted) individuals (irrespective of perceivers' own experience with depression) may depend on perceivers' beliefs about the affective impact associated with suffering from depression (distress), rather than their specific stigma-related beliefs (seriousness). Future research should investigate this possibility.

There are several limitations to the current study that reduce the overall generalizability of our findings. First, using difference scores in Studies 1 and 2 limited the interpretability of our results. Although we intentionally used difference scores to control for individual differences that would affect treatment recommendations for any disorder (e.g., an inclination to perceive all illnesses as being serious), an important consequence of this decision is that our findings can be interpreted only in the context of migraines. For instance, it would not be accurate to posit that Study 1 suggests that perceptions that depression is a serious illness predict treatment recommendations. Rather, our findings show that perceptions that depression is a more serious illness than migraines predict greater willingness to recommend treatment for depression than for migraines. It is worth noting

that results from Study 1 hold when we used the depression ratings without the difference scores.⁶ Our rationale for using difference scores in the current study was based on the assumption that people tend to view depression as being different from disorders with more “physical” symptoms. This assumption was verified by the findings in the current studies.

Relatedly, instead of using difference scores for our analyses, we could have also controlled for perceivers’ migraine ratings in our regressions. However, because we had based our power analyses for Study 1 on the six predictor variables we tested in the regression (bias, familiarity, and four stigma beliefs about depression), we were underpowered to conduct a regression with five additional predictors (e.g., beliefs and familiarity toward migraines). That said, the same pattern of results emerged when the Study 1 regression was run, predicting treatment recommendations for depression without using difference scores but instead including migraines as predictors in the model.

A third limitation in the current investigation is that Study 2 only examined White participants. This was because prior work suggests that stigma interacts with attitudes toward treatment seeking differently as a function of perceivers’ race (e.g., Brown et al., 2010; Givens et al., 2007) and ethnicity (e.g., Georg Hsu et al., 2008; Rao et al., 2007). Although Study 1 included some non-White participants, the findings are unchanged when analyzed with only White participants (see footnote 2). Thus, although our results may speak to effects relevant to White college students (our target population), we cannot speak to whether or not they generalize to other populations. Future research should extend these findings to other racial and ethnic groups as well as to other age groups.

The current studies enhance our knowledge of the manner in which initial evaluations influence important outcomes such as nondepressed individuals’ treatment recommendations. Although future work should extend these findings to clinical populations, our results provide the initial characterization of how stigma affects treatment-seeking intentions. Even though the individuals in the current study had never experienced depression, assessing how stigma affects their treatment-seeking intentions directly informs efforts to reduce effects of stigma on endorsing treatment. The present research identified a link between neural activity reflective of greater engagement of impression formation processes when evaluating depressed individuals and subsequent mental health treatment recommendations. Importantly, because increased engagement of impression formation has been implicated in increased humanization of stigmatized targets (e.g., Harris & Fiske, 2006), these findings may inform the development of future interventions that promote more positive beliefs about mental health treatment (e.g., emphasizing depression’s seriousness). Such an intervention has the ability to significantly improve the quality of life and well-being of individuals suffering from depression.

⁶Predicting treatment recommendations for depression (without using the difference scores) from the four beliefs (seriousness, responsibility, threat, and changeability) when controlling for familiarity and bias is significant, $F(6, 68) = 5.31, p < .001$, and accounted for 33.2% of the overall variance. When predicting seriousness from sympathy and distress using the depression ratings in Study 1 (without using difference scores), the model is significant, $F(2, 69) = 30.35, p < .001$, and accounted for 47.5% of the overall variance (compared to 24% when using the difference scores).

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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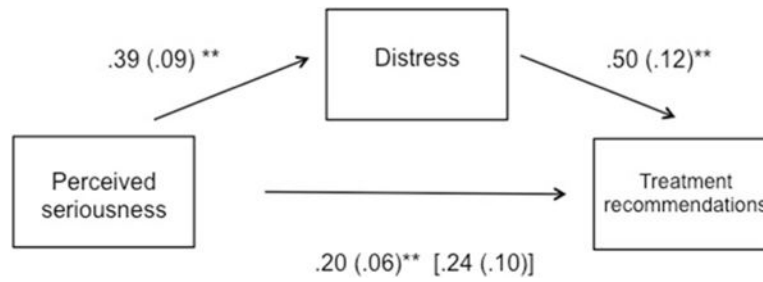


Fig. 1. Results from a mediation analysis demonstrating that participants' beliefs that depression is a more distressing condition than migraines mediated the relationship between their perceptions that depression (versus migraines) is serious and willingness to recommend mental health treatment

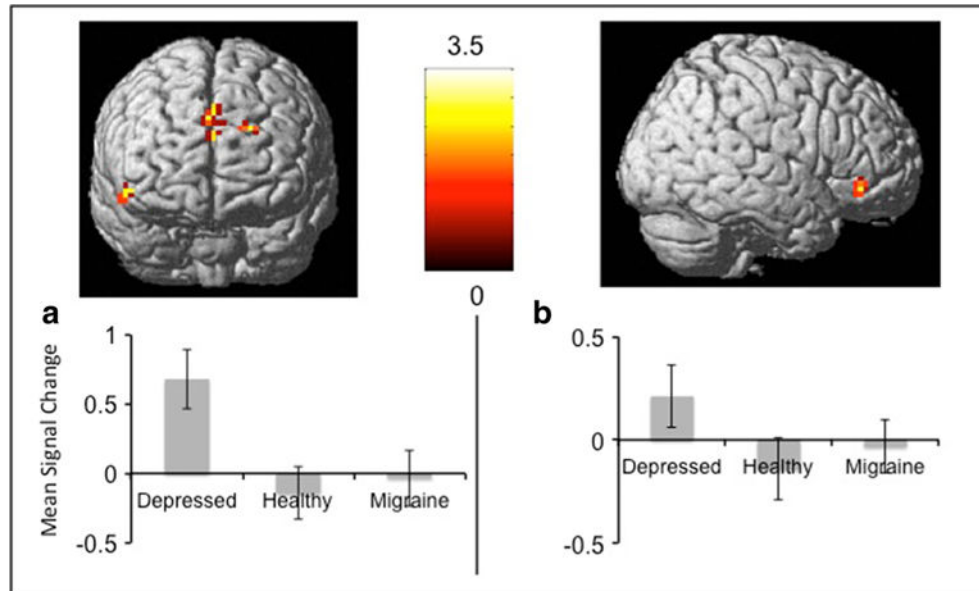


Fig. 2. Anterior and lateral views of the main effects emerging from the whole brain voxel-wise three-way ANOVA (Depression, Migraines, Healthy), $p < .05$ corrected. Subsequent region-of-interest analyses plotted for the dmPFC (a) and vIPFC (b). Error bars are SEM

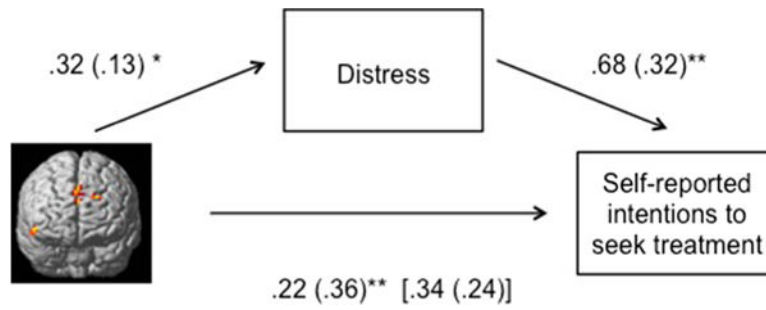


Fig. 3.

Results from a mediation analysis demonstrating that participants' beliefs that depression is a more distressing condition than migraines mediated the relationship between neural activity in the dorsomedial prefrontal cortex (in response to viewing a depressed individual as compared to an individual suffering from migraines) and self-reported treatment seeking intentions

Table 1

Summary of regression predicting willingness to recommend mental health treatment

Variable	β	t	R .550	R^2 .303
Internalized stigma	.116	1.076		
Personal Familiarity	.115	1.042		
Perceived seriousness	.395	3.581**		
Perceived changeability	-.064	-.546		
Perceived responsibility	-.123	-1.102		
Perceived threat	.204	1.781 [^]		

Note. Betas reflect difference scores (depression – migraines),

[^] $p < .10$;

** $p < .005$

Table 2

Main effects from whole-brain voxel-wise ANOVA

Brain region	x	y	z	Kextent	t score
<i>Depressed > Healthy + Migraines</i>					
Left superior frontal gyrus (BA 9)	-21	60	30	18	4.27
Right vIPFC (BA 47)	51	36	-9	17	4.11
Right dmPFC (BA 9)	3	36	33	35	4.01
Left middle frontal gyrus (BA 47)	-48	36	-3	21	3.7
Left vIPFC (BA 47)	-42	18	-12	10	3.97
Left cuneus (BA 18)	-3	-84	18	612	5.72
Right cuneus (BA 17)	9	-81	9	*	5.21
Right posterior cingulate (BA 30)	15	-63	12	*	5.19
<i>Healthy > Depressed + Migraines</i>					
Right insula (BA 13)	33	-3	15	14	5.6
Left parahippocampal gyrus (BA 36)	-33	-27	-21	11	4.91
Left inferior occipital gyrus (BA 18)	-36	-90	-6	15	4.04
Left lingual gyrus (BA 17)	-12	-96	-9	14	3.91
<i>Migraines > Depressed + Healthy</i>					
No significant voxels					

Organized from anterior to posterior.

* indicates subclusters. $p < .001$ uncorrected, 10 voxel extent threshold, all coordinates Montreal Neurological Institute

Table 3
T tests comparing (a) depressed versus migraines; (b) depressed versus healthy; and (c) migraines versus healthy

Brain region	x	y	z	Kextent	<i>t</i> score
<i>a Depressed > Migraines</i>					
Left superior frontal gyrus (BA 9)	-21	60	30	26	4.33
Right dmPFC (BA 8)	12	39	45	26	4.88
Right vIPFC (BA 47)	51	36	-15	44	5.49
Left dmPFC (BA 8)	-15	36	54	10	3.93
Left vIPFC (BA 11/47)	-42	33	-3	23	4.06
Left superior frontal gyrus (BA 6)	-12	15	60	20	4.97
Left middle frontal gyrus (BA 6)	-42	9	51	28	4.52
Left caudate	-18	-3	18	38	5.11
Right middle temporal gyrus (BA 22)	57	-45	3	10	4.29
Left precuneus (BA 7)	-6	-60	30	70	5.89
Left angular gyrus (BA 39)	-48	-60	33	53	4.83
Right posterior cingulate (BA 30)	18	-66	9	380	5.39
Right cerebellum	30	-66	-18	20	4.26
Right cerebellum	60	-81	-15	10	4.77
<i>Migraines > Depressed</i>					
No significant voxels					
<i>b Depressed > Healthy</i>					
Left superior frontal gyrus (BA 9)	-21	60	30	26	4.33
Right dmPFC (BA 8)	12	39	45	26	4.88
Right vIPFC (BA 47)	51	36	-15	44	5.49
Left dmPFC (BA 8)	-15	36	54	10	3.93
Left vIPFC (BA 11/47)	-42	33	-3	23	4.06
<i>Healthy > Depressed</i>					
No significant voxels					
<i>c Migraines > Healthy</i>					
No significant voxels					
<i>Healthy > Migraines</i>					

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Brain region	x	y	z	Kextent	t score
Left putamen	-21	-9	12	29	5.29
Left cuneus (BA 23)	-9	-72	12	17	4.67

$p < .001$ uncorrected, 10 voxel extent threshold, all coordinates Montreal Neurological Institute