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Religiosity and treatment response to antidepressant medication: a prospective multi-site clinical trial

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The present study examined the relationship between religiosity/spirituality and treatment response to antidepressant medication (citalopram). One-hundred and forty-eight Caucasian and African-American adults with uncomplicated major depression were treated with citalopram (20–60 mg/day) over an eight-week period in a prospective multi-site clinical trial. Treatment response was assessed weekly with the Hamilton Rating Scale for Depression. Religiosity (i.e., religious behaviours) and spirituality (i.e., spiritual well-being) were assessed at week 3. No significant associations between spirituality and treatment response were found; however, there was a strong curvilinear relationship between religiosity and treatment response. Compared to lower or higher levels of religiosity, a moderate level of religiosity was significantly associated with a higher likelihood of remission and greater reduction in severity of depression. This association was independent of social support, ethnicity, gender, education, and baseline depression severity. A moderate amount of religiosity appears to be independently associated with an enhanced treatment response to citalopram.

Keywords: religiosity; spirituality; depression; antidepressant; citalopram

Introduction

Over the past two decades, the relationship between religiosity, spirituality,[1] and mental health has become an increasingly important topic of scientific inquiry. Specifically, researchers have examined whether religiosity and spirituality enhance psychological resilience under high stress and whether either serve to protect against the onset of psychiatric disorders or facilitate recovery from these disorders. Although findings are mixed, evidence has begun to emerge suggesting that religiosity and spirituality might promote mental health by protecting against the onset of depression in populations contending with both acute and chronic stressors (see Idler et al., 2003 for review; Smith, McCullough, & Poll, 2003).

In studies of heart surgery patients, patients diagnosed with a terminal illness, men with severe disabilities, recent widowers, and parents who had lost a child, those with

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spiritual resources had lower levels of depression than those without such resources (Ai, Dunkle, Peterson, & Bolling, 1998; Idler & Kasl, 1992; McIntosh, Silver, & Wortman, 1993; Nelson, Rosenfeld, Breitbart, & Galietta, 2002; Siegel & Kuykendall, 1990). Additionally, in a large community sample of older adults, greater religiosity was associated with lower levels of depression (Roff et al., 2004). Husiani, Blasi, and Miller (1999) found a similar negative association between religiosity and levels of depression in older adults, but this relationship was fully mediated by social support. In addition, several systematic reviews of the literature have concluded that religiosity and spirituality measured in various ways are reliably associated with lower levels of depression, at least in cross-sectional analysis (Koenig, McCullough, & Larson, 2001; McCullough & Larson, 1999). Finally, in a large meta-analysis (174 studies, $N = 98{,}975$), religiosity/spirituality was modestly, but reliably associated with lower severity of depressive symptoms (omnibus effect size $= -0.096$) (Smith et al., 2003).

A comparatively small body of research has examined the roles that religiosity and spirituality play in recovery from depression. In a sample of elderly individuals ($N = 177$), the relative importance of religion in one's life (i.e., religious salience) was positively associated with improvement of depression over a one- year period for those who were clinically depressed at baseline (Braam, Beekman, Deeg, Smit, & van Tilburg, 1997). In a 48-week longitudinal study with medically ill, older patients ($N = 94$), intrinsic religiosity (i.e., the degree to which one believes that their religiousness has value in and of itself) (Allport & Ross, 1967), but not religious behaviours (e.g., church attendance, prayer), was predictive of more rapid remission of depression (Koenig, George, & Peterson, 1998). In their sample, every 10-point increase in intrinsic religiosity was associated with a 70% increase in the speed of remission. These results were independent of quality of life, change in functional status during follow-up, family psychiatric history, number of medical diagnoses, social support, and treatment with antidepressant medication. Based on the results of these studies, the association between religiosity, spirituality, and improvement of depression might depend in part on the operational definition of these constructs and the characteristics of the population being studied, but overall, evidence suggests that both resources might promote improvement.

Although the evidence for an association between religiosity, spirituality, and lower levels of depression is compelling, there is a dearth of research examining potential mediators of this relationship. Many theorists have advanced social support as a mechanism that might be a primary mediator of the relationship between religiosity, spirituality, and mental health outcomes (Joiner, Perez, & Walker, 2002). Social support is known to have a positive influence on psychological well-being (Cohen & Wills, 1985) and many individuals might access this resource through religious involvement. Most major world religions promote pro-social behaviour and the cultivation of harmonious, supportive relationships with others (Roberts & Robins, 2000; Saroglou, Delpierre, & Dernelle, 2004). In addition to religious doctrines that encourage supportive relationships, religion might provide direct access to social support via the local religious congregation. For example, the local congregation often provides fellowship opportunities for believers and might serve as a source of emotional and instrumental social support in times of hardship. In the case of the major organised religions, the faithful are given access to a vast, sometimes international, network of individuals who share a world-view, have similar values, and could potentially provide support (see Hill & Pargament, 2003 for a review). Although, social support appears to be an important mediator between religiosity, spirituality, and psychological adjustment, these resources might still have salutary effects even when social support is controlled (Levin, Markides, & Ray, 1996).

The relationship between religiosity, spirituality, and depression might be moderated by ethnicity. It is well attested in the literature that African-Americans tend to be more religiously active than Caucasian-Americans (Ellison, 1995). Indeed, some research suggests that the relationship between religiosity, spirituality, and lower levels of depression might be stronger for African-Americans than Caucasian-Americans (Musick, Koenig, Hays, & Cohen, 1998); however, a large meta-analysis of the literature linking religiosity and spirituality to depression failed to find significant moderation of this relationship by ethnicity (Smith et al., 2003). If ethnicity does moderate this relationship, perhaps the observed moderation is the result of between-group differences in the practice of certain salutary religious behaviours or differential exposure to spiritual beliefs that might serve as a protective factor against depression.

The empirical evidence suggests that religiosity and spirituality have a robust cross-sectional association with lower levels of depression and these resources might also play a role in speeding up recovery from depression. Additionally, these relationships are likely to be at least partially mediated by social support and might be moderated by ethnicity (Caucasian-Americans as compared to African-Americans). However, surprisingly little is known about whether and how religiosity and spirituality might affect treatment response to antidepressant medication. In fact, to our knowledge, there are no studies that have directly examined whether religiosity and/or spirituality are associated with the effectiveness of pharmacotherapy for depression. Since religiosity/spirituality are important coping resources for a large percentage of Americans (see Idler et al., 2003 for a review), it is important to understand whether and how these resources might enhance or interfere with the efficacy of antidepressant medication.

The purpose of the present study is to investigate whether spirituality and/or religiosity are associated with treatment response to an antidepressant medication (citalopram; CIT) in Caucasian-Americans and African-Americans who were enrolled in a highly structured eight-week clinical trial. We hypothesised, consistent with the evidence of the salutary effects of religiosity and spirituality, that both will be associated with better response to CIT (e.g., greater reduction in the severity of depression symptoms and higher rates of remission). Additionally, since research has demonstrated that increased access to social support might be one mechanism through which religiosity and spirituality affect mental health outcomes (see Hill & Pargament, 2003 for review; Husiani et al., 1999), we also hypothesised that the relationship between religiosity/spirituality and treatment response will be at least partially mediated by social support. Finally, because there is some evidence that African-Americans and Caucasian-Americans respond differently to antidepressant medication (Lin, Poland, & Nakasaki, 1993) and the literature suggests that these two groups might differ in the salience of spirituality and the frequency of certain religious behaviours, we explored whether ethnicity moderates the relationship between religiosity, spirituality, and treatment response.

Methods

Participants

The present study uses a sub-sample of African-American and Caucasian-American adults with non-psychotic major depressive disorder who enrolled in a multi-site, non-randomised clinical trial of CIT and were a part of the intent-to-treat group (i.e., participants who returned for the screening visit, and received at least one dose of medicine). The purpose of the main clinical trial was to examine whether there were

significant ethnic differences in treatment response to CIT. The sub-sample used in the present study ($N = 148$) consists of only those participants from the intent-to-treat group of the main trial who completed the religiosity and spirituality inventories. Participants in the main trial were recruited at each of three mental health clinics enrolling treatment-seeking patients as well as those responding to advertisements. To qualify, participants had to: be men and women between 18 and 70 years of age; self-identified as African-American or Caucasian-Americans, and report that both of their parents and all four of their grandparents also self-identified with the same ethnic group; meet DSM-IV criteria for current major depression; have a Hamilton Rating Scale of Depression (21-item HRDS) (Hamilton, 1960) score of ≥ 17; if of child-bearing potential, women agreed to use effective contraception; and were capable of giving written informed consent.

Additionally, prospective participants were excluded if they reported: a current or lifetime diagnosis of schizophrenia, schizophreniform or schizoaffective disorder, psychotic depression or bipolar disorder; current drug or alcohol abuse or dependence or history of drug or alcohol abuse or dependence within the past six months; unstable medical or neurological conditions that were likely to interfere with the treatment of depression; history of allergic reaction to CIT; history of failure of response to CIT, as documented by an adequate trial of the medication defined as having been treated with the medication at a dose level of at least 40 mg of CIT per day for at least six weeks; history of or current seizure disorder; pregnancy or breast-feeding; currently on psychotropic medications including antidepressants, antipsychotics, benzodiazepines, or opiates; treatment with fluoxetine or MAOIs in the previous two months; active suicidal ideation of at least a moderate degree, or other safety issues determined by the clinician to not be suitable for inclusion in the study; or currently receiving ongoing psychotherapy.

More than 1000 potential subjects were screened by telephone or face-to-face interview for the main clinical trial and a total of 327 subjects were enrolled, including 184 African-Americans and 143 Caucasians-Americans. The most likely reasons for non-enrolment were: not meeting criteria for major depression; reported significant substance abuse; taking medication not allowed by the protocol; did not want to enrol in a clinical trial; were of mixed race. The intent–to-treat group consisted of 301 participants: 168 African-Americans and 133 Caucasian-Americans.

The sub-sample used in the present study consisted of only those participants from the intent-to-treat group who completed both the religiosity and spirituality measures ($N = 148$) (mean age $= 43$, $SD = 10.7$). The sub-sample was predominantly female (64%), African-American (64%), unmarried/not cohabitating (79%), reasonably well educated (mean years of education $= 14$, $SD = 2.4$) and approximately half were employed. Compared to those who did not complete the religiosity and spirituality inventories, those who did were significantly more likely to be African-American, more likely to be living with a significant other, and more likely to receive dose escalations of CIT during the clinical trial.

Procedures

After describing the study to the participants, written informed consent was obtained. Demographic information, medical and psychiatric history, and physical examination and laboratory tests (complete blood counts, EKG, thyroid and liver function tests, pregnancy test when appropriate), and urine toxicology screen were obtained at screening. Psychiatric diagnoses were obtained by clinically trained interviewers using

the Structured Clinical Interview for DSM-IV Disorders (SCID) (First, Spitzer, Gibbon, & Williams, 1995).

After screening, participants returned for a baseline visit which included a comprehensive battery of clinical and psychosocial measures administered by trained staff in face-to-face private interviews. Severity of depression was assessed at baseline and at weekly intervals throughout the study using the HRSD (Hamilton, 1960). All participants were placed on a placebo for a one-week "washout" period following the baseline assessment and then were placed on CIT for eight weeks. A placebo control group was not included here, because the purpose of the main trial was to investigate possible ethnic differences in response to CIT due to genetic and/or psychosocial factors, not to determine the efficacy of CIT in the treatment of depression. The effectiveness of CIT has been consistently demonstrated in the previous research (see Keller, 2000 for a review).

All participants received an initial dose of 20 mg/day of CIT, which could be increased to 40 mg at week 4 and to 60 mg/day at week 7 if there was lack of efficacy and tolerable side effects. Participants remained free of non-study psychoactive medication throughout the trial except for zolpidem 5 mg, which could be prescribed occasionally for insomnia (not to exceed 2 nights per week). To monitor compliance with the protocol, pill counts were made at each visit. Participants were compensated up to $320, with the amount of pay prorated by number of sessions attended.

Measures

Spirituality

Spirituality (i.e., spiritual well-being) was assessed during week 3 of the study using the Religious Well-being subscale of the Spiritual Well-being Scale (SWB; Paloutzian & Ellison, 1982). This scale consists of 10 items that assess the perceived quality of one's relationship with God/Higher Being. The items are scored on a 6-point Likert-type scale from "strongly disagree" to "strongly agree," and scores range from 10 to 60. Factor analyses of this measure identify two distinct, but highly correlated factors (affiliation with God/Higher Being and alienation from God/Higher Being) (Scott, Agresti, & Fitchett, 1998). The affiliation items assess one's perceived positive relationship with God/Higher Being (e.g., I believe that God/Higher Being loves me and cares about me). The alienation items assess one's perceived distance from God/Higher Being (e.g., I believe that God/Higher Being is impersonal and is not interested in my daily situations). Since these factors were negatively correlated in the current sample ($r = -0.68$), a reliable (Cronbach's $\alpha = 0.95$) sum score was calculated by adding the total score on the affiliation items to the reverse-coded total score of the alienation items.

Religiosity

Religiosity (i.e., religious behaviours) was assessed at week 3 of the study using The Personal Faith subscale of the Religious Involvement Inventory (RII) (Hilty, Morgan, & Burns, 1984). This scale consists of five items that assess the frequency with which participants engage in religious practices (e.g., prayer, attending worship services, etc.). The items are rated on a 4-point Likert-type scale from "seldom/never" to "regularly," and yields a reliable sum score (Cronbach's $\alpha = 0.86$) that ranges from 5 to 20.

Social support

Social support was measured at baseline and post-treatment using a short (5-item) version of a social support scale used by Vinokur and Vinokur-Kaplan (1990), which was adapted from a scale developed by Abbey, Abramis, and Caplan (1985). Participants were asked to list the four most important people to them and to rate each on a 5-point scale (1 = not at all to 5 = a great deal) on the degree to which they received each of the following five aspects of social support: giving useful information or advice, listening, showing care, providing help with specific problems, and providing needed resources. The responses were summed to create a reliable composite score (Cronbach's $\alpha = 0.90$).

Depression

Severity of depression was the primary outcome and was assessed each week using the Hamilton Rating Scale for Depression (HRSD) (Hamilton, 1960). This is a widely used interview measure completed by clinically trained interviewers who received standardised training and rated participants on a 24-item version of the measure. Only the core 17 items that were common across study sites were used in the analyses. Item rating scales are based on either a 3- or 5-point Likert scale, with a rating of 0 indicating that the symptom is absent or within normal limits and the highest rating indicating that the symptom is present and severe. Ratings were summed to form a composite score. Cronbach's alpha and inter-rater reliability have been found to be within an appropriate range (e.g., Cronbach's $\alpha = 0.82$). For purpose of analysis, an HRSD change score (HRSD at their last visit – pre-treatment HRSD) was calculated.

Data analysis

All data were verified and screened for outliers. In order to identify possible covariates, a series of ANOVA and Pearson Correlation analyses were conducted to determine whether demographic and medical/psychiatric history variables co-varied with religiosity or spirituality and the treatment outcome measures. No covariates were identified; thus the findings reported below are independent of age, gender, ethnicity, SES (e.g., employment status, years of education), history of diagnosed physical or psychiatric illness, current physical or psychiatric illness, severity of depression at study entry, final dose of CIT, and rate of attrition from the study.

Results

Spirituality predicting treatment outcomes

The SWB, our measure of spirituality, was administered to 148 participants ($M = 41.2$, $SD = 15.45$). A linear regression revealed that spirituality did not significantly predict reduction in severity of depression (i.e., change in HRSD score from pre-treatment to post-treatment) ($R^2 = 0.001$, $\beta = -0.038$, $p = 0.639$). Binary logistic regressions revealed that spirituality was not a significant predictor of being a treatment responder (i.e., HRSD pre-post change greater than 50%) ($B = 0.014$, $\text{Exp}(B) = 1.014$, $p = 0.195$) or a remitter (i.e., post-treatment HRSD score ≤ 7) ($B = 0.019$, $\text{Exp}(B) = 1.019$, $p = 0.074$).

SWB was converted into tertiles to test for a possible curvilinear relationship with treatment response, but no significant curvilinear relationship was obtained.

Transformations also were attempted to see if alternative ways of measuring spirituality made relationships between SWB and treatment response more apparent, but none of these transformations resulted in any significant results. Therefore, spirituality appears to have no direct relationship with any of the treatment outcomes studied in this sample.

Religiosity predicting treatment outcomes

The RII, our measure of religiosity, was administered to 148 participants ($M = 11.9$, $SD = 4.44$). A linear regression revealed that there was no significant linear relationship between religiosity and reduction in severity of depression ($R^2 = 0.011$, $\beta = -0.103$, $p = 0.212$). Binary logistic regressions revealed that religiosity was not a significant predictor of either being a treatment responder ($B = 0.065$, $\text{Exp}(B) = 1.068$, $p = 0.112$) or a remitter ($B = 0.058$, $\text{Exp}(B) = 1.060$, $p = 0.131$).

However, when RII was converted into a categorical variable by dividing its scores into tertiles, significant relationships were found between religiosity and the outcomes. A univariate ANOVA revealed that religiosity tertile was significantly associated with reduction in severity of depression ($F(2, 145) = 5.483$, $p = 0.005$, $R^2 = 0.07$). Chi-square tests revealed that religiosity tertile was also significantly associated with remission ($\chi^2(2, N = 148) = 8.989$, $p = 0.011$), but not with being a treatment responder ($\chi^2(2, N = 148) = 3.751$, $p = 0.153$). For more detailed information on the relationship between religiosity tertile and demographic, psychosocial, and outcome variables see Tables 1 and 2.

Post-hoc analyses revealed that participants who were in the middle tertile for religiosity evidenced significantly greater reduction in severity of depression than in participants in both the lower tertile ($t(105) = -3.204$, $p = 0.002$) and the higher tertile ($t(85) = -2.200$, $p = 0.031$) (see Figure 1). This indicates that the relationship between religiosity and reduction in severity of depression is curvilinear, which was partially supported by the results of a quadratic regression which yielded a marginally significant curvilinear relationship ($R^2 = 0.037$, $F(2, 145) = 2.808$, $p = 0.064$).

Post-hoc analyses revealed that participants who were in the middle tertile for religiosity were also significantly more likely to remit than participants in the lower tertile

Table 1. Differences between RII tertile groups on continuous variables.

Variable	Low RII *M (SD)* *n = 61*	Moderate RII *M (SD)* *n = 46*	High RII *M (SD)* *n = 41*	*F*
Age	42.0 *(11.77)*	44.3 *(10.29)*	44.5 *(9.41)*	0.91
Years of Education	13.7 *(2.44)*	13.9 *(2.43)*	14.0 *(2.41)*	1.09
Chronic burden	35.9 *(8.88)*	36.9 *(8.23)*	37.2 *(9.09)*	1.91
Spirituality (SWB)	35.6 *(12.04)*	46.4 *(14.29)*	44.1 *(18.42)*	8.04**
Baseline HRSD	20.1 *(4.53)*	21.6 *(5.12)*	21.1 *(5.68)*	1.12
No. of tx weeks completed	7.6 *(1.32)*	7.7 *(1.05)*	7.8 *(0.88)*	0.54
Baseline soc. undermining	20.5 *(8.24)*	21.2 *(7.96)*	21.0 *(9.11)*	0.10
Post-tx soc. undermining	18.6 *(7.04)*	19.7 *(7.79)*	19.8 *(7.66)*	0.32
Baseline soc. support	65.1 *(21.60)*	67.5 *(21.11)*	70.5 *(19.48)*	0.82
Post-tx soc. support	65.9 *(21.14)*	74.6 *(20.72)*	73.8 *(16.11)*	2.49
HRSD change	−10.5 *(6.79)*	−14.9 *(7.14)*	−11.6 *(6.53)*	5.48**

Note: RII = the Religious Involvement Inventory, the measure used to assess religiosity in the present study.
** = $p < 0.01$.

Table 2. Differences between RII tertile groups on categorical variables.

p	Low RII % *n* = 61	Moderate RII % *n* = 46	High RII % *n* = 41	χ^2
Gender (female)	52.5	78.3	65.9	7.663*
Ethnicity (Caucasian)	49.2	30.4	22.0	8.748*
Alcohol use	47.2	32.5	34.3	2.523
Employed	50.0	62.9	38.2	4.188
Married or cohabitating	22.0	17.4	22.5	0.450
HRSD responder	60.7	78.3	68.3	3.751
HRSD remitter	47.5	76.1	56.1	8.989*

Notes: % = the percentage of participants in each RII tertile who fall into the category shown in the left column.
RII = the Religious Involvement Inventory, the measure used to assess religiosity in the present study.
* = $p < 0.05$.

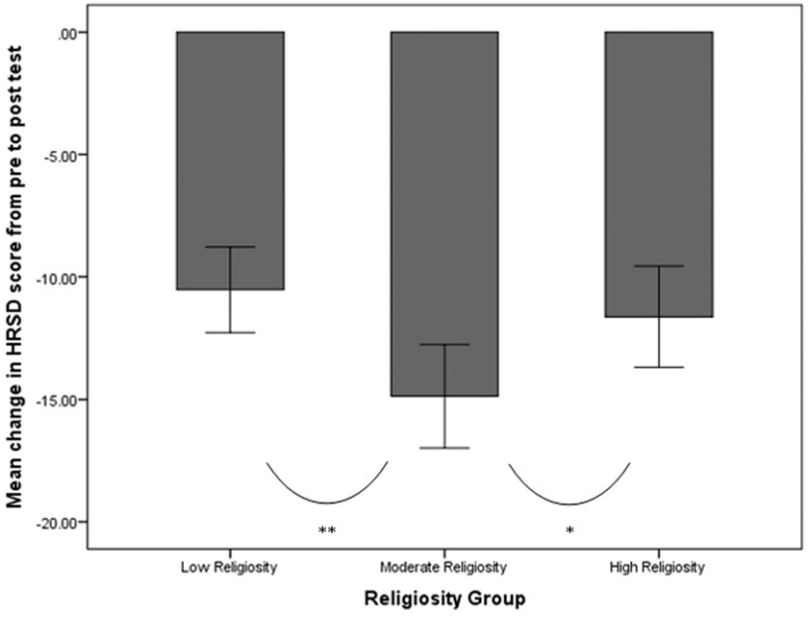

Figure 1. Mean change in HRSD score from pre-treatment to post-treatment by religiosity group. HRSD = Hamilton Rating Scale for Depression, the measure used to assess depression in the present study. Vertical bars depict confidence intervals of 95%. * = difference between groups connected by the arched line is significant at the $p < 0.05$ level. ** = difference between groups connected by the arched line is significant at the $p < 0.01$ level. The mean reduction in severity of depression was significantly greater for the moderate religiosity group than either the low or high religiosity groups.

($\chi^2(1, N = 107) = 8.890$, $p = 0.003$) and the higher tertile ($\chi^2(1, N = 87) = 3.898$, $p = 0.048$) (see Figure 2).

When religiosity was coded as a dummy variable with two levels (''membership in the middle tertile'' and ''membership in the other tertiles''), binary logistic regressions revealed that participants who scored in the middle tertile had approximately three times greater odds of remitting than participants in the other tertiles

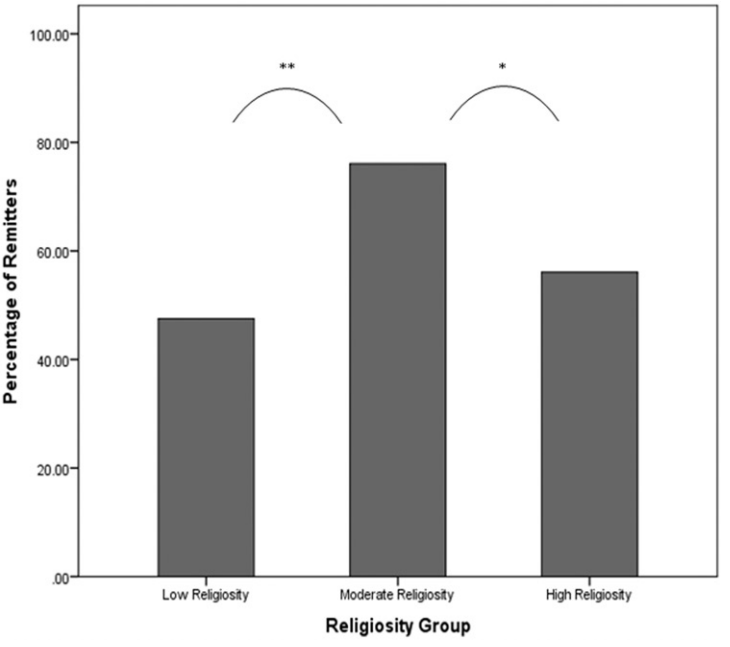

Figure 2. Percentage of remitters (i.e., those with a post-treatment HRSD score of $<$ or $=$ to 7) in each religiosity group. HRSD = Hamilton Rating Scale for Depression, the measure used to assess depression in the present study. * = difference between groups connected by the arched line is significant at the $p < 0.05$ level. ** = difference between groups connected by the arched line is significant at the $p < 0.01$ level. The moderate religiosity group had significantly higher percentage of remitters than either the low or the high religiosity group.

($B = 1.118$, $\text{Exp}(B) = 3.059$, $p = 0.005$). Additionally, individuals who were in the middle tertile were 50% more likely to remit than individuals in the other tertiles. Finally, membership in the middle tertile accounted for approximately 7% of the variance in pre-post HRSD change ($R^2 = 0.066$, $\beta = -0.257$, $p = 0.000$).

Analysis of mediation

Analyses were conducted to test whether the relationship between religiosity and the outcome measures was mediated by social support. In order to test the first step of mediation as established by Baron and Kenney (1986), univariate ANOVA analyses were conducted to determine whether religiosity, as categorised using the aforementioned tertile procedure, was significantly associated with social support. Results showed that religiosity was not significantly associated with social support measured at baseline or post-treatment ($F(2, 140) = 0.817$, $p = 0.444$; $F(2, 111) = 2.488$, $p = 0.088$); therefore, social support does not mediate the relationship between religiosity and treatment response.

Analysis of ethnicity as a possible moderator

We found no ethnic differences (African-American vs. Caucasian-American) in any of the indicators of treatment response to antidepressant medication in our sample as reported in the main trial. However, since religiosity was significantly associated with ethnicity in the

present study (See Table 2), and some research has shown that ethnicity might moderate the association between religiosity and depression (Musick et al., 1998), we explored whether ethnicity moderated the relationship between religiosity and treatment response to CIT. A univariate ANOVA revealed that ethnicity was not a significant moderator of the relationship between religiosity and reduction in severity of depression, $F(2, 143) = 0.189$, $p = 0.828$. A series of Chi-Square tests also revealed that ethnicity was not significantly associated with treatment response in either the lowest RII tertile ($\chi^2(1, N = 61) = 0.794$, $p = 0.373$), the middle RII tertile ($\chi^2(1, N = 46) = 3.111$, $p = 0.078$, or the highest RII tertile ($\chi^2(1, N = 41) = 0.523$, $p = 0.470$). Therefore, ethnicity was not a significant moderator of the relationship between religiosity and overall treatment response in our sample.

We also tested whether ethnicity moderated the relationship between spirituality and treatment response by testing the interaction term (spirituality × ethnicity) using linear regression. Results from this analysis revealed that spirituality × ethnicity was not significantly associated with HRSD change after controlling for the independent effects of spirituality and ethnicity, $R^2 = 0.004$, $\beta = 0.299$, $p = 0.437$. Thus, regardless of how it was tested, ethnicity did not moderate the relationship between spirituality and treatment response.

Discussion

These results show mixed support for our hypotheses. Contrary to expectations, spirituality (i.e., spiritual well-being) was not significantly associated with pre-post reduction in severity of depression, remission from depression or with significant treatment response (≥50% reduction in HRSD score). Therefore, level of spirituality was not significantly associated with treatment response to antidepressant medication in this sample.

On the other hand, religiosity was significantly associated with treatment response in this sample; however, this relationship was more complex than we initially hypothesised. Contrary to the linear relationship that we predicted, we found a curvilinear relationship between these two variables. That is, participants in the study who had moderate levels of religiosity responded significantly better to treatment than those who had either lower or higher levels of religiosity. Specifically, participants who had moderate levels of religiosity were significantly more likely to remit by the end of the clinical trial (50% more likely in this sample) and evidenced significantly greater reduction in severity of their depression, with religiosity accounting for 7% of the variance. This strong relationship appears to be independent of baseline severity of depression, final CIT dose, rate of attrition from study, age, gender, ethnicity, and SES. In addition, ethnicity (African-American vs. Caucasian-American) did not moderate the association between religiosity and treatment response to antidepressant medication in our sample which is consistent with evidence suggesting that ethnicity also does not moderate the relationship between religiosity/spirituality and severity of depression (Smith et al., 2003). Finally, and contrary to expectation, social support did not mediate this relationship.

Based on the results of this study, it appears that engaging in a moderate amount of religious behaviour might be associated with an enhanced treatment response to antidepressant medication. Some researchers posit that religiosity might have positive effects on mental health outcomes because it is associated with increased access to social support and exposure to spiritual beliefs that aid in benefit finding and positive reappraisal coping (Hill & Pargament, 2003); however, religiosity does not appear to be operating through these two mechanisms because religiosity was not associated with social support

and spiritual-well-being was not associated with the treatment outcomes in this study. Perhaps religiosity aids in treatment response by increasing behavioural activation and/or providing additional means (e.g., prayer, meditation, worship service attendance, etc.) to cope with negative mood states. Additionally, some religious practices, such as meditation or prayer, might directly aid in stress reduction by eliciting the "relaxation" response, which is antagonistic to the stress response of the hypothalamic-pituitary-adrenal (HPA) axis (Ai et al., 1998; Delmonte, 1985). Finally, individuals who are more religious might have greater expectancy that medical treatment, including treatment with antidepressants, will be more effective (e.g., a belief that God is working through the medication).

If this finding is replicated, it raises the question as to why a moderate level of religiosity is associated with an enhanced treatment response, but higher or lower levels provide no additive benefit. Since this is the first study of its kind, the literature does not offer a direct answer to this question. We propose two non-mutually exclusive explanations for this relationship.

First, it might be that a greater percentage of participants who reported a higher level of religiosity also belong to religious traditions that passively or actively discourage medical treatments for depression. Thus, these participants might not have derived additional benefits from religious practice because practice itself might expose them to information about their disorder that conflicts with information they receive from their healthcare providers and thereby reduce their expectation that the treatment will be effective and/or elicit feelings of guilt or shame about treating their depression with medication. For example, individuals in the higher religiosity group might be more likely to belong to traditions that believe that depression is a "spiritual" disease as opposed to a psychological disorder. In the Apostle Paul's epistle to the Galatians, he writes that "joy" is one indicator of spiritual health (Galatians 5:19–23, New King James Version). Thus, adherents to religious traditions that interpret this or similar passages literally might believe that the absence of joy (i.e., depression) is an indicator of their "spiritual deficiency" and this belief might promote negative affective states. Unfortunately, this hypothesis could not be tested here, because data on participants' religious beliefs related to depression and religious denomination membership were not collected.

Alternatively, it could be that many individuals who reported higher religiosity in this study might only exhibit high religiosity during times of stress, but return to a low baseline of religious activity after the stress has abated. Thus, these individuals might appear to be highly religious in a cross-sectional design; however, longitudinal research designs would reveal that these individuals exhibit low stable levels of religiosity. Gall, Kristjansson, Charbonneau, and Florack (2009) argue that individuals who exhibit this pattern might not derive benefits from religiosity, because their religious resources are only utilised during times of stress, and are consequently not developed enough to effectively cope with stressors when they arise. In a study of women undergoing biopsies for breast cancer with low pre-morbid spiritual salience, they found that activation of spiritual resources post-diagnosis predicted poorer psychological adjustment six months later. Based on these results, they argue that mobilisation of spiritual resources to cope with a stressor might only be effective if an individual maintains high levels of religious/spiritual salience in the absence of stress. Therefore, it is possible that the higher religiosity group failed to exhibit an enhanced response to treatment because many individuals in this group might have been attempting to activate religious resources that were underdeveloped and ineffective due to infrequent use. Of course, this hypothesis rests upon the assumption that individuals who fit this religious profile are over-represented in the higher religiosity group. Unfortunately, since religiosity was assessed cross-sectionally in this study, we are

unable to test this assumption because we cannot distinguish between individuals who exhibit high temporary religiosity and those who exhibit high stable levels of religiosity.

Another surprising finding was the lack of an association between scores on the SWB (our measure of spirituality) and treatment response to antidepressant medication; however, this finding does not necessarily mean that spirituality has no association with treatment response. The SWB assesses only one dimension of spirituality (the quality of one's relationship with God/Higher Being). Although relationship with and attachment to God/Higher Being has been found to be associated with health (see Hill & Pargament, 2003 for a review), it is possible that this dimension of spirituality is not as relevant to pharmacological treatment response as some other dimensions might be (e.g., spiritual meaning and purpose, health-related faith, etc.). Thus, if a comprehensive, multi-dimensional measure of spirituality were used, an association between some facet of spirituality and treatment response might have been obtained.

Although the results of this study are suggestive, there are several limitations that are important to note. First, because religiosity was assessed cross-sectionally and was not manipulated in this design, we cannot make conclusions about causal relationships. Thus, we can only claim that a moderate amount of religiosity appears to be associated with an enhanced response to antidepressant medication. Second, religiosity was assessed at week 3 instead of at baseline; this methodological limitation introduces the possibility that treatment response might have affected religious behaviour rather than the converse. Third, since this study did not include a placebo control group, it is possible, though unlikely, that the observed ''treatment response'' (e.g., reduction in symptoms, remission) was not due to treatment with CIT, but to some unknown third variable (e.g., spontaneous recovery). In addition, because the study did not include a placebo control group, we cannot conclusively determine from our data whether religiosity is specifically associated with improved response to antidepressant medication or just generally associated with improved recovery from depression. Fourth, since only African-Americans and Caucasians were recruited in this study, it is unknown whether these results will generalise to other ethnic groups. Fifth, the relatively small sample size might have limited power to detect some effects. Finally, since this is the first study to examine the relationship between religiosity, spirituality, and treatment response to antidepressant medication, our findings should be replicated before firm conclusions are made from these results.

In conclusion, a moderate amount of religiosity appears to be associated with improved treatment response to antidepressant medication. The results of the present study highlight the importance of understanding religiosity within the context of treatment for depression. If replicated, these findings could have important implications for clinical practice. For example, clinicians could assess patients' religiosity prior to prescribing antidepressant medication and address religious concerns that might interfere with treatment or promote pre-existing religious behaviour that might benefit treatment. Additional research is also needed to identify some of the biological and psychosocial mechanisms that mediate or moderate this relationship. In future research, religiosity should be assessed longitudinally to determine the direction of causality and to distinguish the effect of acutely activated religiosity (i.e., increase in religious behaviour in response to a crisis) from stable religiosity (i.e., regular religious practices). It is also recommended that researchers employ multi-dimensional measures of religiosity/spirituality to more accurately pinpoint the specific dimensions of religiosity/spirituality that have the strongest associations with treatment response. Finally, additional studies are needed to investigate whether religiosity/spirituality enhances or interferes with treatment response to psychotherapy for depression.

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Note

1. Researchers have yet to agree upon standard operational definitions for the constructs of religiosity and spirituality and there is still some debate as to whether these are distinct or overlapping constructs (Hall, Meador, & Koenig, 2008). In order to avoid confusion in this paper, religiosity is being defined here as behaviours and practices associated with religion (e.g., prayer, church attendance, etc.) and spirituality is being defined here as the existential aspects of religion (e.g., spiritual beliefs, faith, spiritual well-being).

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