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Associations of religious behavior and experiences with extent of regional atrophy in the orbitofrontal cortex during older adulthood

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Abstract

The orbitofrontal cortex (OFC) is a region of the brain that has been empirically linked with religious or spiritual activity, and atrophy in this region has been shown to contribute to serious mental illness in late life. This study used structural magnetic resonance imaging to examine the association between religious or spiritual factors and volume of the orbitofrontal cortex (OFC). Change in the volume of participants' left and right OFC was measured longitudinally over a period of two to eight years. Multiple linear regression analyses showed that religious or spiritual factors were related to extent of atrophy in the left OFC. Significantly less atrophy of the left OFC was observed in participants who reported a life-changing religious or spiritual experience during the course of the study, and in members of Protestant religious groups who reported being born-again when entering the study. Significantly greater atrophy of the left OFC was also associated with more frequent participation in public religious worship. No significant relationship was observed between religious or spiritual factors and extent of atrophy in the right OFC. These results support the presence of a long-term relationship between religious or spiritual experience and brain structure, which may have clinical implications.

Keywords

orbitofrontal cortex; religion; spirituality; regional brain atrophy; older adults

There is growing evidence that religious beliefs and practices may be related to changes in the brain in ways that are directly relevant to mental health outcomes such as depression and cognitive functioning. Studies of brain function have shown that certain areas of the brain may become more active during religious practice (Beauregard & Paquette, 2006; Borg, Andree, Soderstrom, & Farde, 2003; Herzog et al., 1990; Jevning, Anand, Biedebach, & Fernando, 1996; Newberg et al., 2001; Newberg, Pourdehnad, Alavi, & D'Aquili, 2003; Newberg, Wintering, Morgan, & Waldman, 2006; Schjødt, Stødkilde-Jørgensen, Geertz, & Roepstorff, 2008), and that the brains of individuals with certain religious characteristics may react differently in some situations than those of non-religious individuals (Azari, Missimer, & Seitz, 2005; Azari et al., 2001; Han et al., 2008; Harris et al., 2009; Schjødt, Stødkilde-Jørgensen, Geertz, & Roepstorff, 2009). Though evidence for structural

differences in the brain is much more limited, relationships have been identified between religious factors and the volume of certain brain regions measured with magnetic resonance imaging (MRI) (Kapogiannis, Barbey, Su, Krueger, & Grafman, 2009; Owen, Hayward, Koenig, Steffens, & Payne, in press). Using data from an ongoing longitudinal study of changes in structural neuroanatomy in older adults, the present study examines the relationship of religious factors with late life atrophy in the orbitofrontal cortex (OFC), a process that is related in turn to depression (Ballmaier et al., 2004) and dementia (McEvoy et al., 2009).

Religion and the brain

A growing body of neuroimaging evidence supports the concept that religious and spiritual phenomena may be associated with various differences in brain activity, as recent reviews of neuroscience in relation to meditative practices (Cahn & Polich, 2006) and religious and spiritual beliefs more generally (Schjoedt, 2009) have summarized. Change in regional brain activity has been empirically linked to religious or spiritual factors, including prayer (Newberg et al., 2003; Schjødt et al., 2008), meditation (Herzog et al., 1990; Jevning et al., 1996; Lazar et al., 2000; Newberg et al., 2001), recitation of religious texts (Azari et al., 2005; Azari et al., 2001), charismatic religious practices (Newberg et al., 2006), and “self-transcendent” aspects of personality (Borg et al., 2003). Some studies have also found that the brains of individuals with greater levels of religious engagement show different patterns of activity during certain tasks, compared with others. Those who identify as religious may more strongly engage regions associated with cognitive processing during recitation of spiritual texts (Azari et al., 2005; Azari et al., 2001), use social areas of the brain when praying (Schjoedt et al., 2009), and engage different regions when processing self-related information (Han et al., 2008).

Fewer studies have examined the relationship of religion or spirituality with the structure of the brain. However, recent neuroimaging research provides an empirical basis to hypothesize that patterns of brain activity linked with religion/spirituality may have long-term consequences for brain structure. Studies have found that regional gray matter density can be increased over the course of 2 to 12 weeks in response to activities including practicing a motor task (Draganski et al., 2004), learning new academic material (Draganski et al., 2006), and practicing mindfulness-based meditation (Hölzel et al., 2011). Furthermore, research connecting this type of task-related structural change with functional imaging has found the locations in the brain activated during task performance to be the same as those in which structural change later occurs (Ilg et al., 2008), suggesting that habitual patterns of regional brain activity may lead to corresponding changes in neuroanatomy over time. A cross-sectional study exploring religion and structural neuroanatomy found that volumetric differences in certain areas of the temporal and parietal lobes, and the OFC, were associated with individuals’ beliefs about the existence and attributes of God (Kapogiannis, Barbey, Su, Krueger, et al., 2009). Another study found that older adults who reported having life-changing spiritual experiences, and those who belonged to minority religious groups, experienced more severe atrophy of the hippocampus over time (Owen et al., in press).

Despite this range of recent research, there is little consensus regarding which, if any, regions of the brain are most associated with religion. Functional analyses, including those examining functional MRI, PET, and SPECT data, have identified activity related to religious or spiritual factors in the hippocampus (Lazar et al., 2000), temporal lobe (Britton & Bootzin, 2004; Dewhurst & Beard, 1970; Lazar et al., 2000), cingulate gyrus (Newberg et al., 2001), and various parts of the prefrontal (Han et al., 2008; Harris et al., 2009; Newberg

et al., 2001; Newberg et al., 2003; Schjødt et al., 2008) and orbitofrontal (Beauregard & Paquette, 2006; Lou et al., 1999; Newberg et al., 2001) cortices.

Because religion is a complex social and psychological construct, it is reasonable to hypothesize that it also has a multifaceted relationship with regions of the brain (Atran & Norenzayan, 2004; Boyer, 2001). Different types of brain function likely to be involved in religion include cognition (specific beliefs and worldviews), engagement in social systems (perceived relationships with spiritual beings, religious group identification, and dynamic interaction with other group members), affective experiences (feelings of being connected with the divine), and participation in specific behaviors (ritual practices). Furthermore, many religious practices, such as group worship, may engage multiple elements simultaneously. Thus, it is plausible that affective elements of spiritual experience activate emotional regions, while social elements of religion engage social cognitive areas of the brain.

This multifaceted view is consistent with the state of functional neuroimaging research, which tends to show continuity between religious processes in the brain and non-religious processes involving similar types of social, cognitive, or emotional content (Kapogiannis et al., 2009). However, interpretation of these findings is somewhat limited by methodological issues common to neuroimaging research, such as small sample sizes and non-representative samples.

The orbitofrontal cortex

The orbitofrontal cortex (OFC) is a region of the frontal lobes situated behind and above the eyes. It is believed to play a role in emotional regulation (Price, 1999), the perception of reward and punishment (Murray, O'Doherty, & Schoenbaum, 2007; Rolls, 2000; Wallis, 2007), and certain types of social cognition (Beer, Heerey, Keltner, Scabini, & Knight, 2003; Moll, de Oliveira-Souza, Bramati, & Grafman, 2002; Völlm et al., 2006). Damage to this region is associated with impaired ability to form associations between a stimulus and reward or punishment (Rolls, 2000), and with difficulties making appropriate social judgments (Beer et al., 2003). Atrophy in the OFC has also been linked with the risk of Alzheimer's disease (McEvoy et al., 2009), as well as the development and severity of depression in older adults (Ballmaier et al., 2004; Dotson, Davatzikos, Kraut, & Resnick, 2009; Koolschijn, Haren, Lensvelt-Mulders, Pol, & Kahn, 2009; Lai, Payne, Byrum, Steffens, & Krishnan, 2000; Taylor et al., 2007).

While few studies have specifically examined religion and spirituality in relation to the OFC, evidence has been found linking this region with certain types of experiential religious factors. In a study of Carmelite nuns, increased brain activity was found in the right OFC during self-induced mystical states (Beauregard & Paquette, 2006). Among Tibetan Buddhists, increased brain activation was also observed during meditation in several brain regions, including the OFC (Newberg et al., 2001). In a similar study, however, experienced meditators were found to exhibit distinctive patterns of OFC activity only during normal resting states, rather than during meditation (Lou et al., 1999). In a study of structural neuroanatomy in healthy adults, those reporting angry images of God were found to have significantly lower left OFC volume (Kapogiannis, Barbey, Su, Krueger, et al., 2009). Studies of the cognitive activity involved in reciting texts, however, have not identified the OFC as a region related to engagement with religious content, compared with similar but non-religious material (Azari et al., 2005; Azari et al., 2001). Though far from conclusive (see Schjødt, 2009 for a critical review of the inferences drawn from these studies), this body of evidence is broadly consistent with the idea that the same area of the brain active during emotional and relational experiences is also generally implicated in the emotional

and relational elements of religion or spirituality, but not its cognitive elements (Kapogiannis, Barbey, Su, Zamboni, et al., 2009).

Implications of religion for late-life brain change and mental health

A further challenge in the study of religion and the brain is that religious factors not only vary widely between individuals, but are also prone to dramatic changes within individuals across the life course. The importance of religious beliefs, and engagement in religious behaviors, tends to follow a pattern of dramatic decline between adolescence and early adulthood, followed by gradual increase throughout adulthood, so that across historical periods it is the oldest age cohorts that are the most intensely religious (Levin & Taylor, 1997; Uecker, Regnerus, & Vaaler, 2007). In addition to increased subjective importance later in life, many studies also find that the impact of religion on physical and mental health outcomes is particularly strong for older adults (Idler, McLaughlin, & Kasl, 2009; Koenig, 2007; Strawbridge, Cohen, Shema, & Kaplan, 1997).

Cognitive, developmental, and social factors contribute to the importance of religion in late life, which may also have a role in the ways religion influences the brain. Cognitively, the pattern of increasing religiosity associated with aging might be related to increasing mortality salience, as religious beliefs can be effective at buffering the anxiety associated with anticipating one's death (Jonas & Fischer, 2006; Norenzayan, Dar-Nimrod, Hansen, & Proulx, 2009). Developmentally, as religious individuals move through stages of life, the conceptualization of their relationship with the divine may also undergo changes, which may in turn alter the ways in which religious factors are perceived and experienced (Fowler, 1991; Streib, 2001). Furthermore, religious communities provide opportunities for adults in late life to hold positions of social respect, and to have positive interactions with younger group members that are often very limited in other settings (Idler, 2006). As the social and cognitive meanings of being religious change later in life, their correlates in the brain may change as well.

The consequences of these changes in how religion is related to brain activity and structure may be quite significant, given the known relationship between structural changes in the brain and mental health in older adulthood. As people enter late life, their brains tend to lose neurons, resulting in atrophy in the volumes of specific structures (Raz et al., 2005). Atrophy of the OFC has been linked with deterioration in both mood and cognitive functioning. Several studies have linked low OFC volumes with incidence of depression in older adults (Egger et al., 2008; Taylor et al., 2007), and with extent of sub-clinical depressive symptoms (Dotson et al., 2009). In addition, lower OFC volumes in late life have been found to be associated with dementia (McEvoy et al., 2009; Perry et al., 2006). Thus, articulating the factors that might exacerbate or buffer against regional brain atrophy in older adults has the potential to make an important contribution to the understanding, prevention, and treatment of mental health problems among older adults.

The present study

In this study, the association of religious or spiritual factors with baseline OFC volume, and volume changes over time, was analyzed in a sample of older adults. Religious or spiritual factors assessed include measures of religious or spiritual experience, religious behavior, and group affiliation. Building on evidence from the existing body of research regarding the association of religious or spiritual affect and cognition with brain function and structure, this study focuses on the OFC as one region likely to be involved in some of these processes. To the extent that habitual activation of the OFC is related to religious or spiritual practices and experiences, they may promote more robust regional structure in general, and

help to buffer against age-related atrophy. Therefore, it was hypothesized that greater religiousness, as measured by the extent of religious activity and reported religious or spiritual experiences, would be related to larger OFC volume at baseline, and less atrophy of the OFC over the course of the study. While previous research suggests that the OFC is by no means the only brain region associated with religious experience, this combination of factors makes it a useful focus for the present study.

Methods

Data on neuroanatomical, psychosocial, and religious factors were collected as part of the NeuroCognitive Outcomes of Depression in the Elderly study (NCODE), an ongoing longitudinal study of mental health and brain changes in older adults at Duke University Medical Center (see Steffens et al., 2000 for methodological details of this study). The relationships between the key religion variables and both cross-sectional and longitudinal volume of the orbitofrontal cortex (OFC), controlling for total brain size, demographic, and psychosocial factors, were analyzed using multiple linear regression.

Participants

Recruitment of participants began in 1994 and has continued on an ongoing basis through 2010. The sample consists of older adults (age 58+) living in North Carolina and southern Virginia, including individuals meeting DSM-IV (American Psychiatric Association, 1994) criteria for major depressive disorder and non-depressed participants. Exclusion criteria included concurrent diagnosis of other psychiatric or neurological illness, significant cognitive impairment, substance abuse, and contraindication to MRI.

Procedures

MRI scans were acquired every two years, while psychosocial and religious data were collected annually as part of the Duke Depression Evaluation Schedule (DDES) via structured in-person interviews. The DDES is a composite diagnostic interview instrument, which includes sections of the National Institutes of Mental Health (NIMH) Diagnostic Interview Schedule assessing depression. The DDES also includes religion measures (Koenig et al., 1997), four subscales of the Duke Social Support Index (George, Blazer, Hughes, & Fowler, 1989; Landerman, George, Campbell, & Blazer, 1989), and a scale assessing frequency and severity of stressful life events during the six months preceding the interview (Landerman et al., 1989).

Measurement

Neuroimaging measures—Images were acquired with a 1.5 Tesla whole-body MRI system (Signa, GE Medical Systems, Milwaukee, WI) using a standard head (volumetric) radiofrequency coil. The scanner alignment light was used to adjust the head tilt and rotation so that the axial plane lights passed across the cantho-meatal line and the sagittal lights were aligned with the center of the nose. A rapid sagittal localizer scan confirmed the alignment.

A dual-echo fast spin-echo (FSE) was obtained in the axial plane for morphometric analysis of cerebral structures with the following pulse sequence parameters: relaxation time (TR) = 4000ms, excitement time (TE) = 30, 100ms, +16 kHz full imaging bandwidth, echo train length = 16, with a 256 × 256 matrix, 3-mm section thickness, one excitation per phase encoding increment, and a 20cm field of view. The images were acquired in two separate acquisitions with a 3mm gap between sections for each acquisition. The second acquisition was offset by 3mm from the first so that the resulting data set consisted of contiguous sections with no gaps.

The MR images were transferred to the Duke Neuropsychiatric Imaging Research Laboratory (NIRL) where all image analyses were performed. The basic segmentation (i.e., tissue classification) protocol has been described previously (Byrum et al., 1996; Payne et al., 2002). It uses a NIRL-modified version of MrX software, which was created by GE Corporate Research and Development (Schenectady, NY) and originally modified by Brigham and Women's Hospital (Boston, MA) for image segmentation. Once the brain was segmented into tissue types and the non-brain tissue stripped away by a masking procedure, specific regions of interest were assessed using tracing and connectivity functions. The cerebrum and OFC were traced and masks were created that could be applied to the segmented brain. The anatomic definition and boundaries of OFC have been described previously (Lai et al., 2000). The final step calculated the volumes of each tissue type within each region. Volumes were determined for the cerebral hemispheres, and left and right OFC. Total cerebral volume (including gray matter, white matter, and cerebrospinal fluid) was used as a surrogate for intracranial volume. OFC volume included only gray matter.

All image analysts received extensive training by experienced volumetric analysts. Reliability was established by repeat measurements on multiple MR scans before raters were approved to process study data. Intra-class correlation coefficients (ICCs) were: left OFC = 0.9, right OFC = 0.9 and total cerebral volume = 0.997.

Religious or spiritual experiences—Questions about participants' religious or spiritual experiences, belonging, and behaviors (Koenig et al., 1997) were included in the DDES. Participants were asked about their religious or spiritual experiences with two interview questions. All participants received the item "are you a born-again Christian?" (defined in the interview as "a conversion experience, i.e., a specific occasion when you dedicated your life to Jesus"). A follow-up item was asked only of those who responded that they were not born-again: "have you ever had any other religious experience that changed your life?" By comparing responses to these items at baseline and during subsequent interviews, participants were categorized as: born-again at baseline, other religious or spiritual experience at baseline, born-again during study (i.e., did not report being born-again at baseline, but did at a later interview), other religious or spiritual experience during study (i.e., did not report another life-changing religious or spiritual experience at baseline, but did at a later interview), and no religious or spiritual experience.

Religious behaviors—Interview items measured two types of religious behaviors: private practice and public worship. Frequency of private religious practice was assessed with the item "how often do you spend time in private religious activities, such as prayer, meditation, or Bible study?" on a six-point scale with response options of: "more than once a day;" "daily;" "two or more times a week;" "once a week;" "a few times a month;" or "rarely or never." Frequency of public worship was assessed with the item "how often do you attend church or other religious meetings?" on a six-point scale with response options of: "more than once a week;" "once a week;" "a few times a month;" "a few times a year;" "once a year or less;" or "never".

Religious group affiliation—Based on participants' self-report, religious group affiliation was coded into the following categories: Protestant, Catholic, other religion, and no religion. Because a large majority of participants were Protestants, and because there was a very high degree of overlap between being Protestant and having had a born-again experience, the Protestant group was further divided into born-again and non-born-again subcategories. Protestant participants were classified as born-again if they reported a born-again experience during the baseline interview; otherwise they were placed in the non-born-again Protestant group. A small number of non-Protestant participants who reported a born-again experience were excluded from the present analyses (e.g., born-again Catholics, $n =$

12), in order to maintain the conceptual clarity of the group affiliation and religious or spiritual experience effects.

Covariates—Demographic covariates included sex, age, race, and years of education. In addition, stress and social support measures were included as potentially confounding psychosocial correlates of the effects of religious or spiritual factors. A composite subjective social support variable (on a scale ranging from 1 to 30) was used for these analyses and was created from ten individual questions about one's satisfaction with personal relationships (George et al., 1989; Hays, Steffens, Flint, Bosworth, & George, 2001). Self-reported average degree of stress during the last six months (on a scale ranging from 1 to 10) was used to control for stress level. Lastly, depression status (depressed vs. non-depressed group membership) was included as a covariate (Landerman et al., 1989).

Analyses

A combination of cross-sectional and longitudinal analyses were conducted using multiple linear regression (Kutner, Nachtsheim, & Neter, 2004) on the following dependent variables: left and right OFC volumes at baseline, and extent of change in left and right OFC volumes over the duration of the study. Baseline left and right OFC volumes, expressed in mL, were determined using the volumetry procedures described in the neuroimaging measures section above. Longitudinal change in OFC volume was measured between each participant's baseline and final available MRI (i.e., for a participant who had been in the study for two years, the year two MRI was the final measure; for one who had been in the study for four years, the year four MRI was the final measure, and so forth). Measures of volume change for each side of the OFC were computed by subtracting baseline volume from final volume.

Regression models included all key religious variables and covariates as described in the measurement section above (see also Table 1 for descriptive statistics). Model diagnostics indicated that the distributions of the dependent variables were within acceptable parameters for normality and homogeneity of variance, and did not identify any significant multivariate outliers, indicating that this analytical approach was appropriate for the data (Mertler & Vannatta, 2006).

Results

At the time of data extraction, a total of 428 individuals had at least one available MRI scan, and thus were eligible for cross-sectional baseline analyses. Of these, 328 had been in the study long enough to have at least two waves of brain region volume measurements, and thus could also be included in the longitudinal analyses. Twelve participants were eliminated because of inconsistencies in their responses to the questions about religious affiliation and experience (see methods for religious group affiliation). After listwise deletion due to casewise missing data, 422 participants were left in the baseline sample and 306 participants were left in the longitudinal sample. Descriptive statistics for all key variables are presented in Table 1.

Cross-sectional

Cross-sectional analyses were conducted using linear regression on baseline volume for both the left and right OFC. In both models, all baseline independent variables described in the measures section above were included (life changing RSE, born-again Protestant, Catholic, other religious group, no religious group, private practice, public worship, depression status, age, sex, race, education, social support, stress level). To control for the possibility of bias due to attrition, these analyses were performed both with the full sample of participants who

had a baseline MRI scan and with the subsample of only those participants who were included in the longitudinal analyses. The pattern of results was the same for both the full sample and for the longitudinal subsample. For both samples, there were no significant relationships detected between any of the religious variables and either left or right OFC volume at baseline.

Longitudinal

Longitudinal analyses were conducted for both left and right OFC on the variables measuring regional volume change between the baseline and last available MRI scan. Model coefficients are presented in Table 2. In the left OFC, volume change was positively associated with born-again Protestant affiliation at baseline (i.e., born-again Protestants had less volume loss or atrophy) ($b = 0.50$, $p < .05$, $\beta = 0.16$). Volume change in the left OFC was also positively associated with having a life-changing religious or spiritual experience during the study (i.e., this experience during the study predicted less atrophy) ($b = 0.77$, $p < .05$, $\beta = 0.12$). In contrast, volume change in the left OFC was negatively associated with frequency of public worship (i.e., attendance associated with greater atrophy) ($b = -0.14$, $p < .05$, $\beta = -0.16$). No religious or spiritual factors were found to be associated with volume change in the right OFC.

Discussion

This study found significant relationships between religious or spiritual factors and degree of atrophy of the left OFC in a sample of older adults. These results provide qualified support for the hypothesis that certain elements of religion are linked with beneficial changes in the OFC. Specifically, there were two groups exhibiting significantly less atrophy in the left OFC over the course of the study: those who reported a religious affiliation as born-again Protestants at baseline (when they entered the study), and those who reported having another life-changing religious experience between baseline and the time of their final MRI scan in the study. Frequency of attendance at public worship services at baseline, however, was associated with greater atrophy in the left OFC over time. These results were identified only when change over time was examined. No cross-sectional differences in OFC volume at baseline were associated with these religious or spiritual factors in this sample. Interpretation of these results must necessarily remain speculative, owing to the apparent inconsistencies in findings between left and right hemispheres and between baseline volume and atrophy, and to the lack of a clear biological mechanism linking religious experience with neuroanatomical change. Nevertheless, the findings of this study provide evidence of one way in which religion and spirituality may have an enduring relationship with the structure of the brain.

The pattern of these longitudinal findings could be construed as broadly consistent with results from previous studies regarding religion and the OFC. Factors linked with differences in OFC activity include meditation (Lou et al., 1999; Newberg et al., 2001) and mystical experiences (Beauregard & Paquette, 2006). Differences in OFC volume have also been connected with negative affective perceptions of God (Kapogiannis, Barbey, Su, Krueger, et al., 2009). Conversely, OFC activity was unrelated to religious cognition (Azari et al., 2005; Azari et al., 2001). In the present study, born-again and life-changing religious experiences, which were related to less atrophy in the OFC, can reasonably be seen as experiential and emotionally evocative forms of religiousness, similar to those previously related with OFC function. It is also possible that regional culture plays a role in shaping this set of relationships, as born-again Christianity is a highly socially important religious category in the Southeastern United States. Identifying as born-again may therefore have implications for one's location in the social hierarchy that translate into neurobiological effects that would not necessarily be observed in samples living in other cultural contexts.

These interpretations remain speculative, and further studies of OFC volume and atrophy in older adults from other cultural backgrounds, using more precise measures of religious experience, are needed to explore these possibilities.

In addition, frequency of public worship attendance was found in the present study to be related to greater OFC atrophy. Since certain experiential aspects of religion were controlled for in this attendance effect, one interpretation of these findings is that some aspect of frequent worship may be related to OFC atrophy only in the absence of strong spiritual experiences or affective engagement. Another potential explanation is that individuals with comorbid medical conditions that may increase the likelihood of OFC atrophy (such as heart disease or hypertension) may be more likely to attend worship services as a coping mechanism. However, considerably more research is needed in order to address these hypotheses.

In contrast with previous research in structural neuroanatomy (Kapogiannis, Barbey, Su, Krueger, et al., 2009), religious or spiritual factors were not associated cross-sectionally with OFC volume. As this study used a considerably different set of measures, this may indicate one way in which different facets of religion or spirituality may be related to the brain in substantially different ways. A further possibility is that the effects of these particular religious or spiritual factors have an impact only among older adults, while other factors (such as God image) are more influential among younger adults; hence, differences would be evident only in late life. Similarly, these religious or spiritual factors might be primarily effective at buffering against decline rather than promoting growth, thus their protective impact becomes evident only at the age when rates of atrophy increase substantially. However, it is also possible that there is simply more variability in the baseline measures than in the change measures, as there are more extraneous factors potentially influencing differences in brain region size during the previous several decades than during the few years covered by this study. This may obscure the relatively small effects exhibited by the religious factors in the model. Again, further research is needed to address these possibilities.

Another issue raised by these results is that of laterality. Differences based on religion were observed only in the left OFC, while atrophy in the right OFC was unrelated to the religious factors measured in this study. This fits with the limited existing structural findings, which indicated that differences in one's image of God were related to differences in the volume of only the left OFC (Kapogiannis, Barbey, Su, Krueger, et al., 2009). Functional studies, however, have shown religiously based differences in activity to be bilateral (Lou et al., 1999; Newberg et al., 2001), or in the right OFC only (Beauregard & Paquette, 2006). The cause of these apparent differences remains unknown. Future research using functional imaging techniques could help to address this question by looking for elements of religious or spiritual experience that may be lateralized in the left OFC.

While far from conclusive, the results of the present study have potentially important implications for the understanding of late life mental health outcomes. By connecting two phenomena that have each been independently linked with incidence of depression and dementia in older adults – namely, religion and atrophy of the OFC – these findings raise the possibility of identifying potential biological mediators in the brain for the apparent effects of religiousness on health. If certain aspects of religion serve to buffer against OFC atrophy in late life, and reduced OFC atrophy in turn reduces the likelihood and severity of depression and dementia (Egger et al., 2008; McEvoy et al., 2009), this may help to explain the well-documented finding that more religious older adults experience better mental health (Idler et al., 2009).

Some doubt in this interpretation is raised by the negative relationship observed between change in OFC volume and baseline frequency of attendance at religious worship services. Public worship attendance is a common measure of religiousness and has been found to be related to reduced cognitive decline in older adults (Hill, Burdette, Angel, & Angel, 2006; Reyes-Ortiz et al., 2008; Van Ness & Kasl, 2003). These multidirectional results point to a complex relationship between religion and brain health in older adults; some religious or spiritual elements may have beneficial influences, while others have simultaneous countervailing effects. The final outcomes of such a potential web of effects, in terms of the incidence and severity of depression and dementia, is not yet clear, but this is a promising area for future research.

Limitations of the present study include the lack of specificity in some measures of religion or spirituality. Although an experiential definition was provided to participants during the interview, the notion of being “born-again” may not always be interpreted in terms of the definition provided, but may overlap with strong identification with an evangelical group in which considering oneself born-again is central to group membership. There is also a lack of information about the nature of the “other life-changing spiritual experiences” referred to by participants; this question may have been understood and responded to in a variety of very different ways. Another limitation is the lack of information about key religious changes that may have occurred before baseline measurement, and the timing of such changes. The earlier the experience occurred, the longer the participant would have been exposed to the potential effects of, for example, having had a born-again or life-changing religious or spiritual experience. Finally, the sample used in this study was geographically limited to a particular region in the Southeastern United States, potentially limiting generalizability, particularly given the cultural importance of born-again Christianity in this region.

Nevertheless, this study has considerable strengths in its design and size that underscore the importance of the current findings. The longitudinal sample size of more than 300 participants is exceptionally large for an MRI study, making estimates of both significant and null effects less susceptible to distortion by random variation in the sample. In addition, the collection of longitudinal data assessing changes within individuals across time allows for some of the potential ambiguities regarding the directionality of these effects to be addressed. Comparing religious factors at baseline with changes in brain structure across time makes it less plausible that differences in the brain are the cause of religious experiences, and more plausible that it is the religious factors themselves that are influencing the brain changes observed. Finally, the inclusion of measures of multiple dimensions of religion or spirituality allows for simultaneous investigation of experiential, social, and behavioral elements of this complex set of phenomena. The result is that this study was able to differentiate between experience and behavior in their longitudinal relationship with brain structure, which would have been impossible using simpler global measures of religiousness.

In the broadest terms, this study provides evidence of a relationship between religion or spirituality and physical changes in the brain, drawing on a sample that is considerably larger than has been available in previous research in this area. The finding that changes in the OFC, a region involved in the processing of emotional and social information, was related to affective and social elements of religion or spirituality provides support for the notion that different elements of religion are associated with areas of the brain specific to corresponding functions. In addition, the outcome measure in this study – change in OFC volume in late life – has not previously been examined in relation to religion or spirituality, and the results are convergent with cross-sectional studies of OFC volume (Kapogiannis, Barbey, Su, Krueger, et al., 2009) and OFC activity (Beauregard & Paquette, 2006; Lou et al., 1999; Newberg et al., 2001). This outcome suggests that physical changes in the brain

may be one potential biological mediator of some of the positive relationships that have been found between religious or spiritual factors and mental health in older adults. In conclusion, these results suggest that profound religious experiences and social affiliation, but possibly not religious worship frequency, are related to healthier patterns of brain aging.

References

- American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 4. Washington, DC: Author; 1994.
- Atran S, Norenzayan A. Religion's evolutionary landscape: Counterintuition, commitment, compassion, communion. *Behavioral and Brain Sciences*. 2004; 27:713–730. [PubMed: 16035401]
- Azari NP, Missimer J, Seitz RJ. Religious experience and emotion: Evidence for distinctive cognitive neural patterns. *International Journal for the Psychology of Religion*. 2005; 15(4):263–281.
- Azari NP, Nickel J, Wunderlich G, Niedeggen M, Hefter H, Tellmann L, Seitz RJ. Neural correlates of religious experience. *European Journal of Neuroscience*. 2001; 13:1649–1652. [PubMed: 11328359]
- Ballmaier M, Toga AW, Blanton RE, Sowell ER, Lavretsky H, Peterson J, Kumar A. Anterior cingulate, gyrus rectus, and orbitofrontal abnormalities in elderly depressed patients: an MRI-based parcellation of the prefrontal cortex. *American Journal of Psychiatry*. 2004; 161(1):99–108. [PubMed: 14702257]
- Beauregard M, Paquette V. Neural correlates of a mystical experience in Carmelite nuns. *Neuroscience Letters*. 2006; 405(3):186–190. [PubMed: 16872743]
- Beer JS, Heerey EA, Keltner D, Scabini D, Knight RT. The regulatory function of self-conscious emotion: Insights from patients with orbitofrontal damage. *Journal of Personality and Social Psychology*. 2003; 85(4):594–604. [PubMed: 14561114]
- Borg J, Andree B, Soderstrom H, Farde L. The serotonin system and spiritual experiences. *American Journal of Psychiatry*. 2003; 160:1965–1969. [PubMed: 14594742]
- Boyer, P. Religion explained: The evolutionary origins of religious thought. New York, NY: Basic Books; 2001.
- Britton WB, Bootzin RR. Near-death experiences and the temporal lobe. *Psychological Science*. 2004; 15(4):254–258. [PubMed: 15043643]
- Byrum CE, MacFall JR, Charles HC, Chitilla VR, Boyko OB, Upchurch L, Krishnan R. Accuracy and reproducibility of brain and tissue volumes using a magnetic resonance segmentation method. *Psychiatry Research: Neuroimaging*. 1996; 67(3):215–234.
- Cahn BR, Polich J. Meditation states and traits: EEG, ERP, and neuroimaging studies. *Psychological Bulletin*. 2006; 132(2):180–211. [PubMed: 16536641]
- Dewhurst K, Beard AW. Sudden religious conversions in temporal lobe epilepsy. *British Journal of Psychiatry*. 1970; 117:497–507. [PubMed: 5480697]
- Dotson VM, Davatzikos C, Kraut MA, Resnick SM. Depressive symptoms and brain volumes in older adults: a longitudinal magnetic resonance imaging study. *Journal of Psychiatry and Neuroscience*. 2009; 34(5):367–375. [PubMed: 19721847]
- Draganski B, Gaser C, Busch V, Schuierer G, Bogdahn U, May A. Neuroplasticity: Changes in grey matter induced by training. *Nature*. 2004; 427(6972):311–312. [PubMed: 14737157]
- Draganski B, Gaser C, Kempermann G, Kuhn HG, Winkler J, Buchel C, May A. Temporal and spatial dynamics of brain structure changes during extensive learning. *Journal of Neuroscience*. 2006; 26:6314–6317. [PubMed: 16763039]
- Egger K, Schocke M, Weiss E, Auffinger S, Esterhammer R, Goebel G, Marksteiner J. Pattern of brain atrophy in elderly patients with depression revealed by voxel-based morphometry. *Psychiatry Research: Neuroimaging*. 2008; 164(3):237–244.
- Fowler JW. Stages in faith consciousness. *New Directions for Child and Adolescent Development*. 1991; 52:27–45.
- George L, Blazer D, Hughes D, Fowler N. Social support and the outcome of major depression. *The British Journal of Psychiatry*. 1989; 154(4):478–485. [PubMed: 2590779]

- Han S, Mao L, Gu X, Zhu Y, Ge J, Ma Y. Neural consequences of religious belief on self-referential processing. *Social Neuroscience*. 2008; 3(1):1–15. [PubMed: 18633851]
- Harris S, Kaplan JT, Curiel A, Bookheimer SY, Iacoboni M, Cohen MS. The neural correlates of religious and nonreligious belief. *PLoS ONE*. 2009; 4(10):1–9.
- Hays JC, Steffens DC, Flint EP, Bosworth HB, George LK. Does social support buffer functional decline in elderly patients with unipolar depression? *American Journal of Psychiatry*. 2001; 158:1850–1855. [PubMed: 11691691]
- Herzog H, Lele VR, Kuwert T, Langen KJ, Kops ER, Feinendegen LE. Changed pattern of regional glucose metabolism during yoga meditative relaxation. *Neuropsychobiology*. 1990; 23(4):182–187. [PubMed: 2130287]
- Hill TD, Burdette AM, Angel JL, Angel RJ. Religious attendance and cognitive functioning among older Mexican Americans. *Journal of Gerontology B: Psychological Sciences and Social Sciences*. 2006; 61(1):3–9.
- Hölzel BK, Carmody J, Vangel M, Congleton C, Yerramsetti SM, Gard T, Lazar SW. Mindfulness practice leads to increases in regional brain gray matter density. *Psychiatry Research: Neuroimaging*. 2011; 191(1):36–43.
- Idler, EL. Religion in aging. In: Binstock, RH.; George, LK., editors. *Handbook of aging and the social sciences*. 6. New York, NY: Elsevier Academic Press; 2006. p. 277–300.
- Idler EL, McLaughlin J, Kasl S. Religion and the quality of life in the last year of life. *Journal of Gerontology B: Psychological Sciences and Social Sciences*. 2009; 64B(4):528–537.
- Ilg R, Wohlschläger AM, Gaser C, Liebau Y, Dauner R, Woller A, Muhlau M. Gray matter increase induced by practice correlates with task-specific activation: A combined functional and morphometric magnetic resonance imaging study. *Journal of Neuroscience*. 2008; 28:4210–4215. [PubMed: 18417700]
- Jevning R, Anand R, Biedebach M, Fernando G. Effects on regional cerebral blood flow of transcendental meditation. *Physiology & Behavior*. 1996; 59(3):399–402. [PubMed: 8700938]
- Jonas E, Fischer P. Terror management and religion: Evidence that intrinsic religiousness mitigates worldview defense following mortality salience. *Journal of Personality and Social Psychology*. 2006; 91(3):553–567. [PubMed: 16938037]
- Kapogiannis D, Barbey AK, Su M, Krueger F, Grafman J. Neuroanatomical variability of religiosity. *PLoS ONE*. 2009; 4(9):e7180. [PubMed: 19784372]
- Kapogiannis D, Barbey AK, Su M, Zamboni G, Krueger F, Grafman J. Cognitive and neural foundations of religious belief. *Proceedings of the National Academy of Sciences of the United States of America*. 2009; 106:4876–4881. [PubMed: 19273839]
- Koenig HG. Religion and depression in older medical inpatients. *American Journal of Geriatric Psychiatry*. 2007; 15(4):282–291. [PubMed: 17384313]
- Koenig HG, Hays JC, George LK, Blazer DG, Larson DB, Landerman LR. Modeling the cross-sectional relationships between religion, physical health, social support, and depressive symptoms. *American Journal of Geriatric Psychiatry*. 1997; 5(2):131–144. [PubMed: 9106377]
- Koolschijn PCMP, Haren NEMV, Lensvelt-Mulders GJLM, Pol HEH, Kahn RS. Brain volume abnormalities in major depressive disorder: A meta-analysis of magnetic resonance imaging studies. *Human Brain Mapping*. 2009; 30:3719–3735. [PubMed: 19441021]
- Kutner, M.; Nachtsheim, C.; Neter, J. *Applied linear regression models*. 4. New York, NY: McGraw-Hill; 2004.
- Lai TJ, Payne ME, Byrum CE, Steffens DC, Krishnan KRR. Reduction of orbital frontal cortex volume in geriatric depression. *Biological Psychiatry*. 2000; 48:971–975. [PubMed: 11082470]
- Landerman R, George LK, Campbell RT, Blazer DG. Alternative models of the stress buffering hypothesis. *American Journal of Community Psychology*. 1989; 17(5):625–642. [PubMed: 2627025]
- Lazar SW, Bush G, Gollub RL, Fricchione GL, Khalsa G, Benson H. Functional brain mapping of the relaxation response and meditation. *Neuro Report*. 2000; 11:1581–1585.
- Levin JS, Taylor RJ. Age differences in patterns and correlates of the frequency of prayer. *The Gerontologist*. 1997; 37(1):75–89. [PubMed: 9046709]

- Lou HC, Kjaer TW, Friberg L, Wildschiodtz G, Holm S, Nowak M. A 15O-H2O PET study of meditation and the resting state of normal consciousness. *Human Brain Mapping*. 1999; 7(2):98–105. [PubMed: 9950067]
- McEvoy LK, Fennema-Notestine C, Roddey JC, Hagler DJ, Holland D, Karow DS, Dale AM. Alzheimer disease: Quantitative structural neuroimaging for detection and prediction of clinical and structural changes in mild cognitive impairment. *Radiology*. 2009; 251(1):195–205. [PubMed: 19201945]
- Mertler, CA.; Vannatta, RA. Advanced and multivariate statistical methods: practical application and interpretation. 3. Glendale, CA: Pyrczak Publishing; 2006.
- Moll J, de Oliveira-Souza R, Bramati IE, Grafman J. Functional networks in emotional moral and nonmoral social judgments. *NeuroImage*. 2002; 16(3 Part 1):696–703. [PubMed: 12169253]
- Murray EA, O'Doherty JP, Schoenbaum G. What we know and do not know about the functions of the orbitofrontal cortex after 20 years of cross-species studies. *Journal of Neuroscience*. 2007; 27:8166–8169. [PubMed: 17670960]
- Newberg A, Alavi A, Baime M, Pourdehnad M, Santanna J, d'Aquili E. The measurement of regional cerebral blood flow during the complex cognitive task of meditation: a preliminary SPECT study. *Psychiatry Research: Neuroimaging*. 2001; 106(2):113–122.
- Newberg A, Pourdehnad M, Alavi A, D'Aquili EG. Cerebral blood flow during meditative prayer: preliminary findings and methodological issues. *Perceptual and Motor Skills*. 2003; 97:625–630. [PubMed: 14620252]
- Newberg A, Wintering NA, Morgan D, Waldman MR. The measurement of regional cerebral blood flow during glossolalia: A preliminary SPECT study. *Psychiatry Research: Neuroimaging*. 2006; 148(1):67–71.
- Norenzayan A, Dar-Nimrod I, Hansen IG, Proulx T. Mortality salience and religion: divergent effects on the defense of cultural worldviews for the religious and the non-religious. *European Journal of Social Psychology*. 2009; 39(1):101–113.
- Owen AD, Hayward RD, Koenig HG, Steffens DC, Payne ME. The association between religious factors and hippocampal atrophy in late life. *PLoS ONE*. in press.
- Payne ME, Fetzter DL, MacFall JR, Provenzale JM, Byrum CE, Krishnan KRR. Development of a semi-automated method for quantification of MRI gray and white matter lesions in geriatric subjects. *Psychiatry Research: Neuroimaging*. 2002; 115(1–2):63–77.
- Perry RJ, Graham A, Williams G, Rosen H, Erzinçlioglu S, Weiner M, Hodges J. Patterns of frontal lobe atrophy in frontotemporal dementia: a volumetric MRI study. *Dementia and Geriatric Cognitive Disorders*. 2006; 22:278–287. [PubMed: 16914925]
- Price JL. Prefrontal cortical networks related to visceral function and mood. *Annals of the New York Academy of Sciences*. 1999; 877:383–396. [PubMed: 10415660]
- Raz N, Lindenberger U, Rodrigue KM, Kennedy KM, Head D, Williamson A, Acker JD. Regional brain changes in aging healthy adults: general trends, individual differences and modifiers. *Cerebral Cortex*. 2005; 15:1676–1689. [PubMed: 15703252]
- Reyes-Ortiz CA, Berges IM, Raji MA, Koenig HG, Kuo YF, Markides KS. Church attendance mediates the association between depressive symptoms and cognitive functioning among older Mexican Americans. *The Journals of Gerontology Series A: Biological Sciences and Medical Sciences*. 2008; 63(5):480–486.
- Rolls ET. The orbitofrontal cortex and reward. *Cerebral Cortex*. 2000; 10(3):284–294. [PubMed: 10731223]
- Schjødt U, Stødkilde-Jørgensen H, Geertz AW, Roepstorff A. Rewarding prayers. *Neuroscience Letters*. 2008; 443(3):165–168. [PubMed: 18682275]
- Schjødt U. The religious brain: a general introduction to the experimental neuroscience of religion. *Method and Theory in the Study of Religion*. 2009:21–339.
- Schjødt U, Stødkilde-Jørgensen H, Geertz AW, Roepstorff A. Highly religious participants recruit areas of social cognition in personal prayer. *Social Cognitive and Affective Neuroscience*. 2009; 4:199–207. [PubMed: 19246473]

- Steffens DC, Byrum CE, McQuoid DR, Greenberg DL, Payne ME, Blitchington TF, Krishnan KR. Hippocampal volume in geriatric depression. *Biological Psychiatry*. 2000; 48(4):301–309. [PubMed: 10960161]
- Strawbridge WJ, Cohen RD, Shema SJ, Kaplan GA. Frequent attendance at religious services and mortality over 28 years. *American Journal of Public Health*. 1997; 87(6):957–961. [PubMed: 9224176]
- Streib H. Faith development theory revisited: the religious styles perspective. *International Journal for the Psychology of Religion*. 2001; 11(3):143–158.
- Taylor WD, MacFall JR, Payne ME, McQuoid DR, Steffens DC, Provenzale JM, Krishnan KR. Orbitofrontal cortex volume in late life depression: influence of hyperintense lesions and genetic polymorphisms. *Psychological Medicine*. 2007; 37:1763–1773. [PubMed: 17335636]
- Uecker JE, Regnerus MD, Vaaler ML. Losing my religion: the social sources of religious decline in early adulthood. *Social Forces*. 2007; 85:1667–1692.
- Van Ness PH, Kasl SV. Religion and cognitive dysfunction in an elderly cohort. *The Journals of Gerontology Series B: Psychological Sciences and Social Sciences*. 2003; 58(1):S21–S29.
- Völlm BA, Taylor ANW, Richardson P, Corcoran R, Stirling J, McKie S, Elliott R. Neuronal correlates of theory of mind and empathy: A functional magnetic resonance imaging study in a nonverbal task. *Neuro Image*. 2006; 29(1):90–98. [PubMed: 16122944]
- Wallis JD. Orbitofrontal cortex and its contribution to decision-making. *Annual Review of Neuroscience*. 2007; 30(1):31–56.

Table 1

Descriptive statistics (N = 306)

	Min	Max	Mean	SD
<i>Brain volume</i>				
Left OFC baseline (mL)	2.48	12.22	6.53	1.59
Left OFC final (mL)	1.90	12.09	6.68	1.64
Right OFC baseline (mL)	2.19	12.51	6.94	1.75
Right OFC final (mL)	3.29	13.76	7.02	1.83
Total cerebrum (mL)	875.89	1481.80	1151.66	124.75
<i>Demographics</i>				
Age (yrs)	58	92	69.52	6.71
Time in study (yrs)	1	8	4.22	1.95
Education (yrs)	0	17	14.57	2.51
<i>Psychosocial</i>				
Stress level	1	10	5.01	2.64
Social support	10	28	24.83	3.62
<i>Religiosity</i>				
Private practice	0	5	2.90	1.91
Public worship	0	5	2.95	1.74
	N	%		
<i>Religious experiences and belonging</i>				
Protestant	127	41.5		
Born-again Protestant	112	36.6		
Catholic	24	7.8		
Other religion	22	7.2		
No religion	21	6.9		
Born-again during study	25	8.2		
Other RSE baseline	16	5.2		
Other RSE during study	23	7.5		
<i>Depression status</i>				
Depressed	185	60.5		
Non-depressed control	121	39.5		
<i>Sex</i>				
Male	102	33.3		
Female	204	66.7		
<i>Race</i>				
Asian	3	1.0		
Black	29	9.5		
Native American	1	0.3		
White	263	85.9		
Other race	10	3.3		

Table 2

Regression analyses of religious factors and change in brain region volume (N = 306)

	Left OFC		Right OFC	
	<i>b</i>	(SE)	<i>b</i>	(SE)
Intercept	3.70***	(1.66)	5.77***	(1.89)
<i>Religious experiences and belonging</i>				
Born-again during study	0.10	(0.38)	0.14	(0.43)
Life changing (baseline)	-0.21	(0.39)	0.20	(0.44)
Life changing (new)	0.77*	(0.39)	0.55	(0.44)
Born-again Protestant ^a	0.50*	(0.24)	0.39	(0.27)
Catholic ^a	0.04	(0.34)	-0.05	(0.39)
Other ^a	0.42	(0.38)	0.10	(0.43)
None ^a	0.33	(0.44)	0.05	(0.49)
<i>Religiosity</i>				
Private practice	0.03	(0.06)	0.04	(0.07)
Public worship	-0.14*	(0.06)	-0.16	(0.07)
<i>Covariates</i>				
Depression status	-0.37	(0.28)	-0.11	(0.32)
Total cerebrum volume	-0.001	(0.001)	-0.11	(0.06)
Age	-0.03	(0.01)	-0.12	(0.01)
Duration in study	-0.02	(0.05)	-0.03	(0.06)
Sex (female)	-0.08	(0.24)	-0.02	(0.28)
Race (white)	0.01	(0.25)	0.21	(0.28)
Education	-0.02	(0.04)	0.04	(0.04)
Social support	0.01	(0.03)	0.03	(0.03)
Stress level	0.03	(0.05)	0.05	(0.05)

NOTE: Negative coefficients indicate atrophy/shrinkage, relative to baseline size

^aNon-born-again Protestant is the comparison group* $p < .05$,

100' > d
 p < .001

 p < .10
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