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Effect of a One-Week Spiritual Retreat on Brain Functional Connectivity: A Preliminary Study

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Abstract: Background: Many individuals participate in spiritual retreats to enhance their sense of spirituality or to improve their overall mental and spiritual well-being. We are not aware of any studies specifically evaluating changes in functional connectivity using functional magnetic resonance imaging (fMRI) in individuals undergoing an intense spiritual retreat program. The goal of this study was to determine whether such changes occur as a result of participating in the Spiritual Exercises of St. Ignatius. Methods: We conducted psychological and spiritual measures in conjunction with functional connectivity analysis of fMRI in 14 individuals prior to and following shortly after their participation in a one-week spiritual retreat. Results: Significant changes in functional connectivity were observed after the retreat program, compared to baseline evaluation, particularly in the posterior cingulate cortex, pallidum, superior frontal lobe, superior parietal lobe, superior and inferior temporal lobe, and the cerebellum. Significant changes in a variety of psychological and spiritual measures were identified as result of participation in the retreat. Conclusion: Overall, these preliminary findings suggest that this intensive spiritual retreat resulted in significant changes in brain functional connectivity, and warrants further investigation to evaluate the physiological, psychological, and spiritual impact of these changes.

Keywords: functional connectivity; MRI; meditation; prayer; spirituality; religion



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1. Introduction

Spiritual retreats have become very popular for individuals seeking to create personal spiritual or psychological growth. Spiritual retreat programs have developed in many religious and secular traditions and typically incorporate a variety of elements including rituals, prayer, meditation, and self-reflection. Thousands of people engage in such retreats each year, with yoga and meditation retreats among the most popular for both their spiritual and therapeutic value (Edwards 2012; Hoyez 2007). These retreats are also associated with strong emotional responses, with participants reporting that they experience reductions in stress, anxiety, and depression. In addition, participants commonly report a sense of improved psychological well-being, transformation in the spiritual aspects of their lives, and consequences of the retreat that are life changing (Kennedy et al. 2002; Falkenström 2010; Jacobs et al. 2013). A recent systematic analysis revealed that a variety of retreat programs are associated with both short- and long-term improvements in psychological and spiritual measures (Naidoo et al. 2018). The improvements may also be observed on novices to those experienced with various spiritual practices (Montero-Marín et al. 2016). However,

no research has been published on the neurological effects of intensive retreat programs such as functional connectivity measured using magnetic resonance imaging (fMRI).

Several studies have focused on the effect of meditation practice over a short and long duration of time from days to years. Both structural and functional changes have been reported that are associated with the long-term practice of meditation (Newberg et al. 2010; MacCoon et al. 2014; Saggar et al. 2015). Studies of functional connectivity have detected changes in default mode network structures such as the prefrontal cortex, anterior and posterior cingulate cortices, inferior parietal cortex, and lateral temporal cortex (Jang et al. 2011; Brewer et al. 2011). Other studies have also found changes in functional connectivity between structures in the attention network, salience network, and executive network as a result of meditation programs or retreats (Hasenkamp and Barsalou 2012; Kwak et al. 2020).

More broadly, there have been a number of publications concerning the overall relationship between the brain and religious or spiritual phenomena. Studies have explored the relationship between the brain and mystical experiences, near death experiences, religious symbols effects, and religious beliefs in general (Beauregard and Paquette 2006; Beauregard et al. 2009; Harris et al. 2009; Johnson et al. 2014). This research, sometimes referred to as the field of neurotheology, has provided important information on the intersection between neuroscience and religious studies (Newberg 2010). At this time, it is unclear how far such research might be able to expand the broader understanding of religious and spiritual phenomena. For example, if studies reveal a significant relationship between religious beliefs and emotional centers in the brain, the finding could have implications on the importance of emotions in understanding those beliefs. On the other hand, if data point to more cognitive processes, this could also influence our understanding of the nature of such beliefs.

Previously, we have reported (Newberg et al. 2017) on the dopaminergic and serotonergic changes resulting from a one-week spiritual retreat based upon the Spiritual Exercises developed by St. Ignatius Loyola (1491–1556), founder of the Society of Jesus known as the Jesuits. The Ignatian Spiritual Exercises utilize a variety of elements including living in silence, performing prayer and meditation, and personal reflection. Elements also have a specific Christian perspective focusing on topics during contemplative periods including sin, God’s mercy, the life and passion of Jesus, and God’s love. Throughout the duration of the retreat period, individual guidance is provided by a spiritual advisor to facilitate spiritual growth or personal transformation. The transformation can come in the form of a deeper understanding of the person, of the person’s relationship with God, and of the larger understanding of meaning and purpose in the universe (Salai 2016). Such transformative experiences from the retreat can also be measured using a number of psychological and physiological parameters that reflect long-term effects. We proposed that the Ignatian retreat would be an ideal target for neuroscientific inquiry given its long history, well developed structure, and likelihood of strong spiritual experiences in a relatively short period of time. Thus, in our initial report, we evaluated participants before and after the Ignatian retreat using DaTscan (Ioflupane) single-photon emission computed tomography (SPECT). Interestingly, the results of the study showed a significant reduction in dopamine and serotonin transporter binding after the retreat when compared to the baseline SPECT imaging. Such a change was postulated to be associated with a “priming” of the brain for intense spiritual experiences by enabling the brain to be more affected by the release of serotonin or dopamine. This prior study was the first ever to report such changes in these neurotransmitter systems as a result of participating in a spiritual retreat. Such a finding is also linked to a limited number of other studies that demonstrate the impact during spiritual practices on neurotransmitters such as dopamine and serotonin (Newberg and Yaden 2018). Further, these findings may have implications for their psychological effects since serotonin and dopamine are well known to be associated with changes in mood and affect, found in various disorders such as depression (Amsterdam et al. 2012; Spies et al. 2015).

The present study, on the effects of an Ignatian retreat, takes another step toward a greater understanding of the neurophysiological effects from a structured, prolonged and intense spiritual practice by describing functional connectivity data obtained from the same subjects who were evaluated in our previously published study on serotonin and dopamine transporter imaging. Thus, subjects underwent resting blood oxygen level-dependent (BOLD) magnetic resonance imaging (MRI) before and after they participated in the one-week Ignatian spiritual retreat to observe what longer-standing changes occurred in functional connectivity as a result of undergoing the retreat program. Resting BOLD MRI is a simple technique that acquires imaging over a 5–10 min period in order to assess the MRI signal associated with changes in blood flow and blood oxygenation. When the signal between two brain regions is concordant, they are considered to be functionally connected. Functional connectivity helps show neurophysiological changes associated with different brain states and processes. The changes observed with resting BOLD MRI are distinct from, but can complement, other techniques such as SPECT imaging mentioned above and positron emission tomography (PET) imaging. These latter two techniques involve injecting a radioactive tracer that measures some physiological process in the brain such as cerebral blood flow, metabolism, or neurotransmitter activity.

We hypothesized that given the psychological and spiritual changes anticipated in the retreat, there would be significant changes in functional connectivity in a variety of structures that are associated typically with such practices. Specifically, we hypothesize that areas related to emotional processes that underlie positive feelings such as joy including the limbic system, cerebellum, prefrontal cortex, and basal ganglia, would be significantly different after the retreat. We also expected that areas involved in the default mode network would be different as this area has been shown to be involved with meditation practices. Finally, we hypothesized that there would be significant findings in the dopamine areas of the brain such as the pallidum.

Therefore, the goals of this study were to determine whether the one-week spiritual retreat resulted in changes in functional connectivity and whether any imaging changes related to qualitative changes in psychological or spiritual measures.

2. Methods

2.1. Subjects and Imaging Acquisition

The Thomas Jefferson University Institutional Review Board for human subjects and Radiation Safety reviewed and approved the study protocol and consent form. The subjects were recruited by advertising with local churches and pastoral care departments from the local community. For eligibility, the subjects were permitted to have participated in prior spiritual retreats, but could not have participated previously in an Ignatian-based retreat for one week or longer. All subjects underwent an extensive screening that consisted of their medical and psychiatric history, to ensure that there were no contraindications or risks from the MRI; none of the study subjects had a current disorder, such as stroke, tumor, active cardiac disease, or an Axis I psychiatric disorder that might affect cerebral physiology.

All subjects who participated in this study met the following inclusion criteria: (1) cognitively able to provide informed consent and willingness to complete this study; (2) agreement to attend the one-week spiritual retreat; (3) willing to undergo the full imaging procedures with no metal in their body; and (4) women of childbearing potential with a negative blood or serum pregnancy test.

Subjects were excluded from this study if they had: (1) any neurological or psychiatric disorders, including drug or alcohol abuse, that could interfere with cerebral physiology; (2) any active medical conditions that could interfere with cerebral physiology; (3) currently taking medication(s) (i.e., antidepressants, antipsychotics, anxiolytics, benzodiazepines, sedatives, anti-seizure medications) that could affect cerebral physiology; (4) unable or unwilling to lie still in the scanner; and (5) history of previous brain surgery or intracranial abnormalities that could complicate the interpretation of the brain scans.

Within one month of entering into the one-week spiritual retreat, all subjects completed an initial, evaluation with resting BOLD fMRI along with a completion of a battery of validated psychological and spiritual questionnaires. Afterward, within one week of completing the retreat, the subjects returned for their post retreat evaluation which repeated the resting BOLD fMRI and questionnaires. It should be noted that two subjects received their post retreat scans at 12 and 14 days due to logistical issues with scheduling the scans.

After inclusion and exclusion criteria were met, a total of 14 subjects (8 males and 6 females) were enrolled in this study. The subjects were of ages 24–76 years old with a mean age of 54 ± 13 years with a mean education level of 18.5 ± 1.7 years. All 14 subjects were Christian (7 Catholics, 5 Protestants, 1 Orthodox/Anglican, and 1 Quaker). Eight subjects reported previous experience with different types of religious or spiritual retreats. However, no subject had undergone an Ignatian retreat. Subjects had a low level of depression as a group, with a mean Beck Depression score of 4.4 ± 6.0 (scores below 13 are considered within normal limits) and a moderate amount of anxiety with a mean Spielberger Trait Anxiety score of 29.3 ± 7.2 . We did not control for other variables including measures of religiosity at baseline or prior meditation/retreat experience. However, subjects functioned as their own control and thus we planned to evaluate the general change from baseline for the subjects after the retreat program.

2.2. Retreat Description and Components

The intended purpose of the one-week Ignatian retreat is to create a time for greater understanding of an individual's spiritual life and how to incorporate this new understanding into their everyday life. One goal is to evoke a substantial change and/or deepening of one's spiritual and religious beliefs. All subjects participated in the one-week Ignatian retreat at the Jesuit Center in Wernersville, Pennsylvania. The retreat site is located in a rural area on 240 acres of natural land with beautiful grounds and art. The retreat is performed primarily in silence. On the first day, each retreatant met with a designated retreat director (usually a priest or nun) who would engage in dialogue and provide daily guidance and insights regarding retreat exercises, plan, and direction each retreatant pursued during the retreat. The retreat is based on the Ignatian exercises (Mottola 1964) but does not follow them strictly to allow for responsiveness to each person's retreat experience. The plan for each day consisted of voluntary participation in morning mass with additional time spent extensively in personal reflection, contemplation, and prayer. Each day, a meeting with the spiritual director was planned; meals were eaten in a common dining area with other retreatants that were typically shared in silence.

2.3. Instruments and Measures

Previously, we reported the effect of the retreat on various psychological and spiritual measures, and provided additional background regarding that data so that they might be considered in the context of the functional connectivity results. To summarize briefly, at the time of undergoing the fMRI scans, each participant completed a series of psychological inventories and measures of spirituality. These surveys have been validated originally in large populations and have been used in both clinical and research settings extensively. The battery of psychological and spiritual measures included the following: the Spielberger State Trait Anxiety Inventory (STAI-Y) is a 20 item questionnaire with a four item response to assess symptoms of anxiety (Spielberger et al. 1983); the Profile of Moods States (POMS) is a 37 item questionnaire with a five item response to assess a variety of symptoms associated with tension, anger, vigor, fatigue, depression, and confusion (McNair et al. 1971); the Beck Depression Inventory (BDI) is a 21 item questionnaire with four response items to assess symptoms associated with depression (Beck and Beck 1972); the 12-Item Short Form Health Survey (SF-12) which asks questions associated with general health and well-being (Ware et al. 1996); the Cloninger Self-Transcendence Scale which has 26 questions rated on a 5-point Likert scale (Garcia-Romeu 2010); and the Brief Multidimensional Measure of Re-

ligiousness/Spirituality which is a 38 item scale evaluating 11 dimensions of religiousness and spirituality (Fetzer Institute/National Institute on Aging Working Group 1999).

The MR imaging was performed on a 3T Philips Achieva scanner using a standard 8 channel head coil. Structural MRI brain images were collected using a T1-weighted Magnetization-Prepared Rapid Gradient Echo (MPRAGE) sequence for anatomical localization. The imaging parameters used were: field of view (FOV) = 25.6 cm, voxel size = $1.0 \times 1.0 \times 1.0 \text{ mm}^3$, matrix size = 256×240 , the repetition time (TR) = 6.44 s, and echo time (TE) = 3.16 s, slice thickness = 1 mm, number of slices = 170, flip angle = 8° and acquisition time = 280 s. After this structural scan, resting-state functional MRI (rs-fMRI) data were collected using an Echo Planar Imaging (EPI) sequence using the following parameters: FOV = 25.6 cm, voxel size = $2 \times 2 \times 4 \text{ mm}^3$, matrix size = 128×128 , TR = 2.5 s, TE = 35 ms, slice thickness = 4 mm, number of slices = 34, number of volumes = 120 and acquisition time = 300 s. During the rs-fMRI scan, all subjects were instructed to close their eyes, keep their head still, and relax quietly for approximately 5–6 min.

2.4. Functional Connectivity Image Acquisition and Procedure

In order to process the resting-state BOLD scans, it is important to separate the target low frequency components from physiological noise. The following processing and analysis was performed for the acquired functional volumes in order to uniquely describe the communication between resting-state networks without the effect of noise contaminants. This analysis pipeline is well-established in our institution and widely used in the fMRI community for evaluating rs-fMRI scan data. All resting-state data were spatially preprocessed using SPM12 (Wellcome Department of Cognitive Neurology, University College London, UK) in the Matlab environment (Mathworks, Inc.). Realignment was initially performed to ensure proper voxel to voxel correspondence within the BOLD time series. BOLD is used to differentiate changes in cerebral blood flow (CBF) in fMRI scans and to assess the signal comparison between different structures. The functional volumes from the BOLD fMRI scans were then slice time corrected to account for timing inconsistencies within the EPI data. In order to facilitate the removal (i.e., co-vary out) of confounding temporal factors prior to modeling, scans are segmented into gray matter, white matter, and CSF. Spatial normalization was then performed for each data set and warped to the Montreal Neurological Institute coordinate space through a subject specific deformation field and smoothed with a three dimensional Gaussian kernel with a full width at half maximum (FWHM) of $4 \times 4 \times 8 \text{ mm}^3$. This spatial processing optimizes the data for additional temporal corrections to emphasize the low-frequency resting-state networks of interest for connectivity analysis. The Conn toolbox was integrated into the Matlab environment for component-based noise correction (CompCor) of physiologic and other noise sources such as heart rate or respiratory rate inherent to BOLD imaging.

The preprocessed functional volumes from the prior step were then imported into the Conn toolbox for the resting-state analysis. Structural volumes were separated into white matter, gray matter, and CSF confounds. White matter and CSF confounds were placed in a three-dimensional space and a band-pass filter of 0.008 to 0.09 was applied to restrict analysis to a limited frequency window. For the primary analysis, seed regions of interest (ROI) were used to evaluate specific structures in the frontal, temporal, and parietal lobes, as well as the cerebellum, limbic areas, and cingulate cortex. Changes in functional connectivity between the pre and post retreat scans were analyzed and regions with significant changes reported, corrected using the False Discovery Rate (FDR) method to mitigate against false positives due to multiple comparisons.

3. Results

The results from the functional connectivity analysis are shown in Table 1 and Figure 1. There was significantly increased connectivity between the posterior cingulate and the right superior frontal gyrus and between the posterior cingulate and the left pallidum. There were a number of regions that had significantly reduced connectivity after the retreat.

Areas with significantly reduced connectivity included the left superior parietal lobe and left superior temporal gyrus; the right inferior temporal gyrus and the right supramarginal gyrus; the right cerebellum and right hippocampus; the left cerebellum and the right parahippocampus; and the vermis and the left cuneus. We found no effects associated with age, gender, or education background.

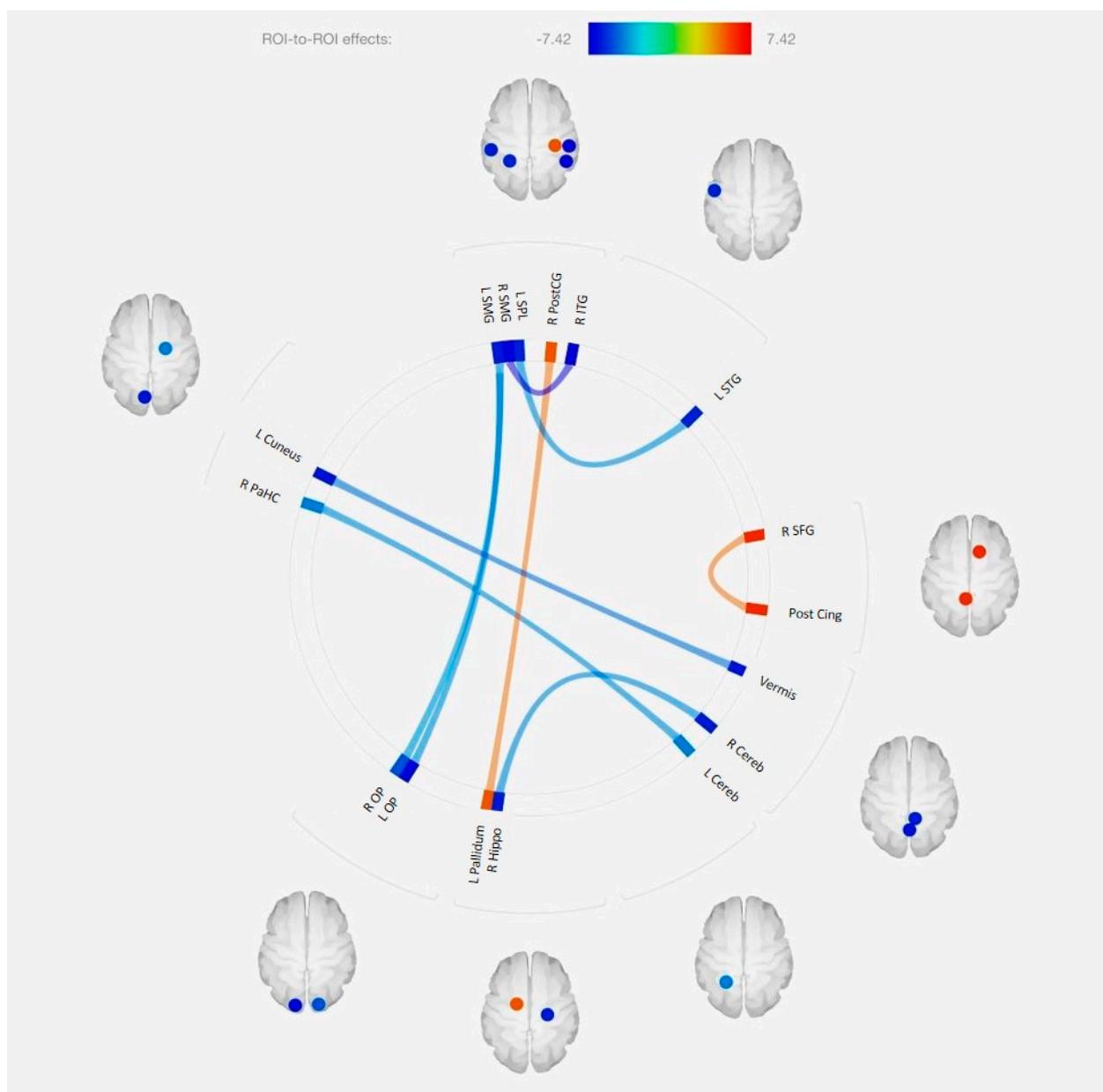


Figure 1. Schematic representation of changes in functional connectivity before and after the one-week spiritual retreat. The colored lines represent the connectivity either increased (red colors) or decreased (blue colors). The lines connect the structures involved and are also described in Table 1. Abbreviations: L = left; R = right; PaHC = parahippocampus; OP = Occipital pole; Cereb = cerebellum; Post Cing = posterior cingulate; SFG = superior frontal gyrus; STG = superior temporal gyrus; ITG = inferior temporal gyrus; PostCG = posterior central gyrus; SPL = superior parietal lobule; SMG = supramarginal gyrus.

Table 1. Results from rsBOLD analysis.

Structures	Statistic	p-unc	p-FDR
Post Cingulate: R SFG	T(13) = 5.37	0.0001	0.017
Post Cingulate: L Pallidum	T(13) = 5.30	0.0001	0.020
L SPL: L STG	T(13) = −4.91	0.0003	0.038
R ITG: R SMG	T(13) = −7.42	0.0000	0.001
R Cerebellum: R Hippocampus	T(13) = −4.99	0.0002	0.033
L Cerebellum: R PaHC	T(13) = −4.90	0.0003	0.039
Vermis: L Cuneus	T(13) = −5.40	0.0001	0.017

There were several significant changes found on the post retreat psychological and spirituality measures (previously reported) that warrant discussion. There were significant changes (decreases) in the measures of tension (6.2 ± 6.1 pre retreat and 2.1 ± 2.2 post retreat, $t(13) = 2.62$, $p = 0.01$) and fatigue (4.4 ± 1.4 pre retreat and 2.7 ± 2.1 post retreat, $t(13) = 2.94$, $p = 0.01$). No other psychological measures were significantly changed. On the Brief Multidimensional Measure of Religiousness/Spirituality, we found statistically significant results in religious and spiritual beliefs (6.7 ± 1.2 pre retreat and 7.4 ± 1.0 post retreat, $t(13) = 1.88$, $p = 0.04$) and increased religiousness and (3.1 ± 0.8 pre retreat and 3.5 ± 0.7 post retreat, $t(13) = 2.69$, $p = 0.01$) and spirituality (3.6 ± 0.5 pre retreat and 3.9 ± 0.4 post retreat, $t(13) = 1.88$, $p = 0.04$). A significant increase in feelings of self-transcendence was found on the Cloninger Self-Transcendence Scale (18.2 ± 9.0 pre retreat and 20.1 ± 6.0 post retreat, $t(13) = 2.42$, $p = 0.01$). It should be noted that we did not find significant correlations between the qualitative measures and imaging findings.

4. Discussion

This is the first study that has measured changes in functional connectivity using fMRI with participants in an intensive Ignatian retreat program. The findings, while preliminary, suggest that participation in a spiritual retreat of this type can have a short-term impact on the functional connectivity in brain regions believed to be associated with religious and spiritual practices and experiences. Specifically, structures such as the superior frontal cortex, limbic system, cingulate gyrus, superior temporal lobe and parietal regions have all been found to be involved in meditation- and prayer-based programs both in the short and long term.

It is important to note that the Ignatian has multiple elements including meditation, silence, prayer, self-reflection, and personal spiritual guidance which can all potentially affect brain function (Newberg and Iversen 2003). In recent years, meditation practices have been studied and have been found to elicit a number of neurophysiological and subjective changes. The literature and our previous research has utilized (fMRI), positron emission tomography (PET), and single-photon emission computed tomography (SPECT) to evaluate changes in cerebral blood flow and brain activation during meditation and prayer states (Wang et al. 2011; Garrison et al. 2014; Kwak et al. 2020). The measurable changes reported in the literature depend in large part on the types of the meditation practice and associated experiences (Newberg and Iversen 2003). Generally the findings in functional neuroimaging research suggests that there is a network in the brain associated with religious or spiritual practices that include changes in the attentional system including the prefrontal cortex, cingulate gyrus, and superior parietal lobes. Changes in activity appear in the limbic areas such as the amygdala, hippocampus, and thalamus.

It is also important to emphasize that numerous studies have reported that spiritual practices such as the ones involved in the Ignatian retreat improve a number of physical and mental health related measures. For example, various systematic reviews and meta-analyses have demonstrated that religious involvement by itself is associated with lower morbidity and mortality (McCullough et al. 2000; Oman et al. 2002). Imaging studies such as the current one might help elucidate the mechanism by which such effects could occur.

Studies focusing on meditation-based practices have demonstrated a significant benefit for patients with disorders such as hypertension, psoriasis, irritable bowel disease, epilepsy, and hormonal related symptoms (Ooi et al. 2017; Arias et al. 2006; Gamret et al. 2018). The benefit might come in the form of helping with coping through such problems or in actually improving various clinical measures.

When it comes to mental health, studies have shown religious beliefs to be associated with improvements in anxiety and depression symptoms (Captari et al. 2018; Smith et al. 2003; Braam et al. 1999). Meditation-based practices have consistently demonstrated improvements in depression and anxiety (Li and Bressington 2019; Jain et al. 2007). Even specific prayer-based practices such as performing the Rosary have been found to reduce anxiety symptoms (Anastasi and Newberg 2008). In the present study, the subjects were found to have significant improvements in measures of tension and fatigue along with the expected increases in religious and spiritual beliefs. The mechanism by which spiritual beliefs and practices likely are associated with psychological and neurophysiological changes are supported by the current research. Brain structures such as the cerebellum and limbic regions are known to be involved in the expression and modulation of emotions. Thus, finding changes in these areas after an intensive spiritual retreat help to clarify how the components of the retreat affect brain processes that lead to psychological changes (Yaden and Newberg 2018; Newberg and Yaden 2018).

The results from this preliminary study suggest that there are structures with both increased and decreased functional connectivity in the brain. For example, functional connectivity was increased between the posterior cingulate gyrus and the superior frontal gyrus and the left pallidum. Both the superior frontal gyrus and posterior cingulate may be associated with self-awareness since the posterior cingulate is a structure in the self-processing component of the default mode network (Goldberg et al. 2006). Since a substantial element of the Ignatian retreat is spent in self-reflection and silence, an increased connectivity between these two structures could be consistent with such a subjective response.

The second relationship is particularly relevant with respect to previous findings that showed changes in dopaminergic function when comparing the pre and post retreat results the retreat program. Increased connectivity between the pallidum, the primary dopaminergic region, and the posterior cingulate could reflect how dopamine augments the self-awareness process (Joensson et al. 2015; Lou et al. 2017). It is also possible that dopamine supports a more positive outlook on the self. All of the participants reported significant increases in the manner in which they viewed their own self.

Several other structures had reduced connectivity as a result of participation in the retreat. Of note, there was reduced connectivity between the cerebellum and limbic structures such as the hippocampus and parahippocampus. There is increasing evidence that the cerebellum may be particularly involved in the coordination of emotional processes, particularly negative ones (Utz et al. 2015). The cerebellum connects with the limbic structures both ipsilaterally and contralaterally (Cacciola et al. 2017). It has also been found that the vermis may be particularly connected to the limbic structures (Blatt et al. 2013). Diminished connectivity could reflect a more positive emotional response of the individuals, which was reported in terms of reduced depression and anxiety. More importantly, in a spiritual context, the retreat enabled participants to reflect on personal growth positive affective responses which allow for less regulation of negative emotions by the cerebellum. It should be noted that we did not find significant correlations between the qualitative psychological or religious measures and imaging findings, in part due to the small sample size and in part due to the number of comparisons that would have to be made. Furthermore, there was a great deal of uniformity in the subject group with all but two individuals expressing elevated levels of stress or depression. Given the low initial levels of these measures, it was unlikely to be able to assess substantial changes in these measures. However, the results from this study can provide a basis for future, larger studies, that can better assess the

relationship between areas of the brain affected by these retreat programs and various subjective, psychological responses.

Decreased connectivity between the superior parietal lobe and superior temporal gyrus could be consistent with our prior hypothesis that these areas are involved in fostering a sense of connectedness and oneness that are characteristic expressions of spiritual experiences. We have proposed that diminished neuronal input into these regions would result in a diminished spatial sense of the self, leading to a sense of oneness (Newberg and Iversen 2003). This is distinct from the self-reflection associated with the posterior cingulate and pallidum described above.

One important limitation of this pilot study is that there was no comparison group in the sense of having other subjects go through one or more different types of meditation programs. Although we would expect test-retest effects to be minimal in a pure control group (i.e., doing nothing in between evaluations), it is reasonable to conclude that participation in other types of retreats, ranging in duration of time and intensity, could yield similar findings as those that we report here. Or different practices could yield a different set of physiological effects. Meditation programs such as Mindfulness-Based Stress Reduction (MBSR) and Kirtan Kriya meditation research conducted by the authors (Monti et al. 2012) have resulted in neurophysiological and clinical changes which shared some similarities in terms of affecting the frontal and temporal lobes. However, there are also distinctions between practices both in terms of their respective elements and outcomes. Based upon the feasibility and findings of this preliminary study, we hope that our future research will be able to utilize an active control group and one or more comparison groups to study cohort effects and the many different elements and sources of systematic variance.

One goal of the retreat in the current study is to gain an understanding of how practices incorporated into everyday life can produce substantial change. Such findings are consistent with the activation in brain structures that had altered functional connectivity. The decreased functional connectivity with parietal lobe structures and superior temporal lobe may be associated with differentiation of their self-orienting functions resulting in a feeling of oneness or self-transcendence (Newberg and Iversen 2003). Functional connectivity changes associated with the dopamine areas of the pallidum might also be associated with alterations in the brain associated with religious and spiritual practices or experience (Kjaer et al. 2002).

In this study, we did not attempt to differentiate the effects of the various elements of the retreat. It is possible that non-spiritual factors may have been important contributors to the findings such as simply taking time off from work and daily stressors, being in a vacation-like environment, or spending time in nature. Future studies will need to try to delineate which factors are most effective and related to the changes in brain function.

Another issue with our findings is that we might be evaluating the effect of emotional or spiritual experience rather than the effect of the retreat. The practice of prayer could result in changes in the brain. However, the subjective experience associated with that prayer could result in similar brain changes. Given these limitations, it is important to develop future studies to determine the key factors of retreats, both spiritual and secular, to determine whether there are similar effects. The literature has shown longitudinal changes in brain function associated with prolonged exposure to meditation retreats and practices (Newberg et al. 2010; MacCoon et al. 2014; Saggar et al. 2015).

Regarding our study design, the subject selection also raised important methodological challenges for this study and future studies. To begin, since this was a preliminary study, it did not have a sufficient number of subjects to find relationships between other variables such as gender, age, or level of education. However, it was a relatively uniform population in terms of these variables which limits the ability to detect significant effects on the response to the retreat program. We also did not control for baseline measures of religiosity, previous participation in retreats, or level of religious or spiritual practice. In terms of the meditation experience of the subjects, we enrolled subjects with reasonable experience with meditation or spiritual practices. However, it was not clear who would make the

best subjects for this retreat study. On one hand, novice individuals might be expected to have a more intense spiritual experience since they have never participated in such a program before. However, people with too little experience with spiritual practices or retreats, might be overwhelmed or confused by the retreat program. They might not be able to engage in the retreat program as fully as someone who was more familiar with the specific elements. Since our goal was to observe the effect of the retreat program rather than assess how different types of individuals might experience it, we decided to not make the level of prior spiritual involvement an inclusion criteria for enrollment. Thus, our only exclusion criterion was that the study subjects were not permitted to have previously participated in this specific Ignatian Spiritual Exercises retreat. However, future studies might be able to explore the effects of age or gender that might contribute to the impact of the retreat. Younger individuals typically have a greater capacity for neuroplasticity, and hence, may derive more change from various training programs such as a spiritual retreat. Women tend to be more likely to engage in meditation practices, but both men and women have found such practices similarly beneficial (Upchurch and Johnson 2019).

Since the retreat has a Christian perspective, and all participants identified as Christians, there was an inherent bias towards having a positive experience in the retreat. It is important to develop future study designs that can reduce the participants' personal beliefs and biases and enroll a diverse group of participants to include persons from different traditions in order to be generalizable to the general population.

Overall, these preliminary data represent changes in functional connectivity using fMRI associated with an Ignatian retreat. This preliminary study contributes to the existing literature on the study of meditation, prayer and the associated interconnected networks in the brain that are activated by these practices.

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Abbreviations

R	right
L	left
SFG	superior frontal gyrus
STG	superior temporal gyrus
ITG	inferior temporal gyrus
PaHC	parahippocampus
SMG	supramarginal gyrus
p-unc	the uncorrected p value
p-FDR	the p value corrected for multiple comparisons using the False Discovery Rate method

References

- Amsterdam, Jay D., Andrew Newberg, Irene Soeller, and Justine Shults. 2012. Greater striatal dopamine transporter density may be associated with major depressive episode. *Journal of Affective Disorders* 141: 425–31. [CrossRef] [PubMed]
- Anastasi, Matthew W., and Andrew B. Newberg. 2008. A Preliminary Study of the Acute Effects of Religious Ritual on Anxiety. *Journal of Alternative and Complementary Medicine* 14: 163–65. [CrossRef] [PubMed]
- Arias, Albert J., Karen Steinberg, Alok Banga, and Robert L. Trestman. 2006. Systematic Review of the Efficacy of Meditation Techniques as Treatments for Medical Illness. *Journal of Alternative and Complementary Medicine* 12: 817–32. [CrossRef] [PubMed]
- Beauregard, Mario, Jérôme Courtemanche, and Vincent Paquette. 2009. Brain activity in near-death experiencers during a meditative state. *Resuscitation* 80: 1006–10. [CrossRef]
- Beauregard, Mario, and Vincent Paquette. 2006. Neural correlates of a mystical experience in Carmelite nuns. *Neuroscience Letters* 405: 186–90. [CrossRef]
- Beck, Aaron T., and Roy W. Beck. 1972. Screening Depressed Patients in Family Practice. *Postgraduate Medical Journal* 52: 81–85. [CrossRef]
- Blatt, Gene J., Adrian L. Oblak, and Jeremy D. Schmahmann. 2013. Cerebellar Connections with Limbic Circuits: Anatomy and Functional Implications. In *Handbook of the Cerebellum and Cerebellar Disorders*. Berlin: Springer Science and Business Media LLC, pp. 479–96.
- Braam, Arjan, Aartjan T. Beekman, Dorly J. Deeg, Jan H. Smit, and Willem Van Tilburg. 1999. Religiosity as a protective factor in depressive disorder. *The American Journal of Psychiatry* 156: 809.
- Brewer, Judson A., Patrick D. Worhunsky, Jeremy R. Gray, Yi-Yuan Tang, Jochen Weber, and Hedy Kober. 2011. Meditation experience is associated with differences in default mode network activity and connectivity. *Proceedings of the National Academy of Sciences of the United States of America* 108: 20254–59. [CrossRef]
- Cacciola, Alberto D. Demetrio Milardi, Alessandro Calamuneri, Lilla Bonanno, Silvia Marino, Pietro Ciolli, Margherita Russo, Daniele Bruschetta, Antonio Duca, Fabio Trimarchi, Angelo Quartarone, and et al. 2017. Constrained spherical deconvolution tractography reveals cerebello-mammillary connections in humans. *Cerebellum* 16: 483–95. [CrossRef]
- Captari, Laura E., Joshua N. Hook, William Hoyt, Don E. Davis, Stacey E. McElroy-Heltzel, and Everett L. Worthington Jr. 2018. Integrating clients' religion and spirituality within psychotherapy: A comprehensive meta-analysis. *Journal of Clinical Psychology*, 1938–51. [CrossRef]
- Edwards, Tamala M. 2012. Get Thee to a Monastery. *Time Magazine*. Available online: <http://content.time.com/time/magazine/article/0,9171,139669,00.html> (accessed on 1 September 2020).
- Falkenström, Fredrik. 2010. Studying mindfulness in experienced meditators: A quasi-experimental approach. *Personality and Individual Differences* 48: 305–10. [CrossRef]
- Fetzer Institute/National Institute on Aging Working Group. 1999. *Multidimensional Measurement of Religiousness/Spirituality for Use in Health Research: A Report of the Fetzer Institute/National Institute on Aging Working Group*. Kalamazoo: John E. Fetzer Institute.
- Gamret, A. Caresse, Alexandra Price, Raymond M. Fertig, Hadar Lev-Tov, and Anna J. Nichols. 2018. Complementary and Alternative Medicine Therapies for Psoriasis. *JAMA Dermatology* 154: 1330–37. [CrossRef] [PubMed]
- García-Romeu, Albert. 2010. Self-transcendence as a measurable transpersonal construct. *Journal of Transpersonal Psychology* 42: 26–47.
- Garrison, Kathleen A., Dustin Scheinost, R. Todd Constable, and Judson A. Brewer. 2014. BOLD signal and functional connectivity associated with loving kindness meditation. *Brain and Behavior* 4: 337–47. [CrossRef] [PubMed]
- Goldberg, Ilan I., Michal Harel, and Rafael Malach. 2006. When the Brain Loses Its Self: Prefrontal Inactivation during Sensorimotor Processing. *Neuron* 50: 329–39. [CrossRef] [PubMed]
- Harris, Sam, Jonas T. Kaplan, Ashley Curiel, Susan Y Bookheimer, Marco Iacoboni, and Mark S. Cohen. 2009. The Neural Correlates of Religious and Nonreligious Belief. *PLoS ONE* 4: e7272. [CrossRef]
- Hasenkamp, Wendy, and Lawrence W. Barsalou. 2012. Effects of Meditation Experience on Functional Connectivity of Distributed Brain Networks. *Frontiers in Human Neuroscience* 6: 38. [CrossRef]
- Hoyez, A. C. 2007. The 'world of yoga': The production and reproduction of therapeutic landscapes. *Social Science & Medicine* 65: 112–24.
- Jacobs, Tonya L., Phillip R. Shaver, Elissa S. Epel, Anthony P. Zanesco, Stephen R. Aichele, David A. Bridwell, Erika L. Rosenberg, Brandon G. King, Katherine A. Maclean, Baljinder K. Sahdra, and et al. 2013. Self-reported mindfulness and cortisol during a Shamatha meditation retreat. *Health Psychology* 32: 1104–9. [CrossRef]
- Jain, Shamini, Shauna L. Shapiro, Summer Swanick, Scott C. Roesch, Paul J. Mills, Iris Bell, and Gary E. R. Schwartz. 2007. A randomized controlled trial of mindfulness meditation versus relaxation training: Effects on distress, positive states of mind, rumination, and distraction. *Annals of Behavioral Medicine* 33: 11–21. [CrossRef]
- Jang, Joon H., Wi Hoon Jung, Do-Hyung Kang, Min Soo Byun, Soo Jin Kwon, Chi-Hoon Choi, and Jun Soo Kwon. 2011. Increased default mode network connectivity associated with meditation. *Neuroscience Letters* 487: 358–62. [CrossRef]
- Joansson, Morton, Kristine Rømer Thomsen, Lau M. Andersen, Joachim Gross, Kim Mouridsen, Kristian Sandberg, Leif Østergaard, and Hans C. Lou. 2015. Making sense: Dopamine activates con-scious self-monitoring through medial prefrontal cortex. *Human Brain Mapping* 36: 1866–77. [CrossRef] [PubMed]

- Johnson, Kyle D., Hengyi Rao, Nancy Wintering, Namisha Dhillon, Siyuan Hu, Senhua Zhu, Marc Korczykowski, Katrina Johnson, and Andrew B. Newberg. 2014. Pilot study of the effect of religious symbols on brain function: Association with measures of religiosity. *Spirituality in Clinical Practice* 1: 82–98. [CrossRef]
- Kennedy, James, R. Anne Abbott, and Beth S. Rosenberg. 2002. Changes in spirituality and well-being in a retreat program for cardiac patients. *Alternative Therapies in Health and Medicine* 8: 64–73. [PubMed]
- Kjaer, Troels W., Camilla Bertelsen, Paola Piccini, David Brooks, Jørgen Alving, and Hans C. Lou. 2002. Increased dopamine tone during meditation-induced change of consciousness. *Cognitive Brain Research* 13: 255–59. [CrossRef]
- Kwak, Seoyeon, So-Yeon Kim, Dahye Bae, Wu-Jeong Hwang, Kang Ik Kevin Cho, Kyung-Ok Lim, Hye-Yoon Park, Tae Young Lee, and Jun Soo Kwon. 2020. Enhanced Attentional Network by Short-Term Intensive Meditation. *Frontiers in Psychology* 10: 3073. [CrossRef] [PubMed]
- Li, Simon Yat Ho, and Daniel Bressington. 2019. The effects of mindfulness-based stress reduction on depression, anxiety, and stress in older adults: A systematic review and meta-analysis. *International Journal of Mental Health Nursing* 28: 635–56. [CrossRef]
- Lou, Hans, Jean-Pierre Changeux, and Astrid Rosenstand. 2017. Towards a cognitive neuroscience of self-awareness. *Neuroscience & Biobehavioral Reviews* 83: 765–73. [CrossRef]
- MacCoon, Donal G., Katherine A. MacLean, Richard J. Davidson, Clifford D. Saron, and Antoine Lutz. 2014. No Sustained Attention Differences in a Longitudinal Randomized Trial Comparing Mindfulness Based Stress Reduction versus Active Control. *PLoS ONE* 9: e97551. [CrossRef]
- McCullough, Michael E., William T. Hoyt, David B. Larson, Harold G. Koenig, and Carl Thoresen. 2000. Religious involvement and mortality: A meta-analytic review. *Health Psychology* 19: 211–22. [CrossRef]
- McNair, Douglas, Maurice Lorr, and Leo F. Droppleman. 1971. *POMS Manual for the Profile of Mood States*. San Diego: Educational and Industrial Testing Service.
- Montero-Marín, Jesus, Marta Puebla-Guedea, Paola Herrera-Mercadal, Ausias Cebolla, Joaquim Soler, Marcelo Demarzo, Carmelo Vazquez, Fernando Rodríguez-Bornaetxea, and Javier García-Campayo. 2016. Psychological Effects of a 1-Month Meditation Retreat on Experienced Meditators: The Role of Non-attachment. *Frontiers in Psychology* 7: 1935. [CrossRef]
- Monti, Daniel A., Kathryn M. Kash, Elisabeth J. S. Kunkel, George Brainard, Nancy Wintering, Aleezé S. Moss, Hengyi Rao, Senhua Zhu, and Andrew B. Newberg. 2012. Changes in cerebral blood flow and anxiety associated with an 8-week mindfulness programme in women with breast cancer. *Stress and Health: Journal of the International Society for the Investigation of Stress* 28: 397–407. [CrossRef] [PubMed]
- Mottola, Anthony. 1964. *The Spiritual Exercises of Saint Ignatius*. New York: Image Books.
- Naidoo, Dhevaksha, Adrian Schembri, and Marc M. Cohen. 2018. The health impact of residential retreats: A systematic review. *BMC Complementary and Alternative Medicine* 18: 1–17. [CrossRef] [PubMed]
- Newberg, Andrew B. 2010. *Principles of Neurotheology*. Surrey: Ashgate Publishing Ltd.
- Newberg, Andrew B., and David B. Yaden. 2018. The Neurobiology of Meditation and Stress Reduction. In *The Neurobiology of Meditation and Stress Reduction*. New York: Oxford University Press (OUP), pp. 97–117.
- Newberg, Andrew B., and Jeremy Iversen. 2003. The neural basis of the complex mental task of meditation: Neurotransmitter and neurochemical considerations. *Medical Hypotheses* 61: 282–91. [CrossRef]
- Newberg, A. B., N. Wintering, D. B. Yaden, L. Zhong, B. Bowen, N. Averick, and D. A. Monti. 2017. Effect of a one-week spiritual retreat on dopamine and serotonin transporter binding: A preliminary study. *Religion, Brain & Behavior* 8: 265–78. [CrossRef]
- Newberg, Andrew B., Nancy Wintering, Dharma S. Khalsa, Hannah Roggenkamp, and Mark R. Waldman. 2010. Meditation effects on cognitive function and cerebral blood flow in subjects with memory loss: A preliminary study. *Journal of Alzheimer's Disease* 20: 517–26. [CrossRef]
- Oman, Doug, John H. Kurata, William J. Strawbridge, and Richard D. Cohen. 2002. Religious attendance and cause of death over 31 years. *International Journal of Psychiatry in Medicine* 32: 69–89. [CrossRef]
- Ooi, Soo Liang, Melisa Giovino, and Sok Cheon Pak. 2017. Transcendental meditation for lowering blood pressure: An overview of systematic reviews and meta-analyses. *Complementary Therapies in Medicine* 34: 26–34. [CrossRef]
- Saggar, Manish, Anthony P. Zanesco, Brandon G. King, David A. Bridwell, Katherine A. MacLean, Stephen R. Aichele, Tonya L. Jacobs, B. Alan Wallace, Clifford D. Saron, and Risto Miiikkulainen. 2015. Mean-field thalamocortical modeling of longitidinal EEG acquired during intensive meditation training. *Neuroimage* 114: 88–104. [CrossRef]
- Salai, Sean S. J. 2016. Father James Martin: An introduction to Ignatian contemplation. *America Magazine*, September 21.
- Smith, Timothy B., Michael E. McCullough, and Justin Poll. 2003. Religiousness and depression: Evidence for a main effect and the moderating influence of stressful life events. *Psychological Bulletin* 129: 614–36. [CrossRef]
- Spielberger, Charles D., Richard L. Gorsuch, Robert Lushene, P. R. Vagg, and Gerald A. Jacobs. 1983. *Manual for the State-Trait Anxiety Inventory*. Palo Alto: Consulting Psychologists Press.
- Spies, Marie, Gitte M. Knudsen, Rupert Lanzenberger, and Siegfried Kasper. 2015. The serotonin transporter in psychiatric disorders: Insights from PET imaging. *The Lancet Psychiatry* 2: 743–55. [CrossRef]
- Upchurch, Dawn M., and Pamela Jo Johnson. 2019. Gender Differences in Prevalence, Patterns, Purposes, and Perceived Benefits of Meditation Practices in the United States. *Journal of Women's Health* 28: 135–42. [CrossRef] [PubMed]
- Utz, A., Markus Thüring, Thomas M. Ernst, Andrea Hermann, Rudolf Stark, O. T. Wolf, and Christian Merz. 2015. Cerebellar vermis contributes to the extinction of conditioned fear. *Neuroscience Letters* 604: 173–77. [CrossRef]

-
- Wang, Danny J.J., Hengyi Rao, Marc Korczykowski, Nancy Wintering, John Pluta, Dharma Singh Khalsa, and Andrew B. Newberg. 2011. Cerebral blood flow changes associated with different meditation practices and perceived depth of meditation. *Psychiatry Research: Neuroimaging* 191: 60–67. [[CrossRef](#)] [[PubMed](#)]
- Ware, John E., Mark Kosinski, and Susan D. Keller. 1996. A 12-Item Short-Form Health Survey. *Medical Care* 34: 220–33. [[CrossRef](#)] [[PubMed](#)]
- Yaden, David B., and Andrew B. Newberg. 2018. The Interaction of Religion and Health. In *The Interaction of Religion and Health*. New York: Oxford University Press (OUP).