Field Analysis of the Neuroscientific Study of Religious and Spiritual Phenomena

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Introduction

With the rapidly expanding field of research exploring religious and spiritual phenomena, there have been many perspectives regarding the validity, importance, relevance, and need for such research. There is also the ultimate issue of how such research should be interpreted with regard to epistemological questions. The best way to evaluate this field is to determine the methodological issues that currently affect the field and explore how best to address such issues so that future investigations can be as robust as possible and make this body of research more mainstream.

It should also be mentioned at the outset that the overall study of religious and spiritual phenomena requires at its root, an analysis of very complex, very compelling, and very subjective experiences. Hence the field of cognitive neuroscience offers one of the most important fields of study to explore such phenomena. It is unfortunate that various perspectives regarding this research are often uninformed or misinformed regarding the nature and potential results of such research. Perspectives range from the highly religious to the highly materialistic with concerns from "writing off" religious experience on one hand to being unimportant on the other. These criticisms miss several major issues such as the challenge to cognitive neuroscience for exploring arguably some of the most complex mental phenomena human beings have. With many current studies on emotion, laughter, morality, and happiness being reported almost daily, there should also be substantial information regarding complex human experiences vis a vis the study of religious and spiritual phenomena. Furthermore, it is a great challenge to science to develop appropriate definitions, measurement tools, and methods in order to study such phenomena. The results from these studies will also provide important mechanistic data that may help elucidate any potential health effects, positive or negative, that are associated with religion and spirituality. The religious and spiritual perspectives also stand to gain tremendously from this interaction since the results might help towards a new and deeper understanding of these phenomena. This research may also lead to a better understanding not only of specific types of experiences, but of a wide range of phenomena that pertain to religion including love, altruism, charity, forgiveness, worship, theology, and epistemology. However, it should be stated that such leaps must be made carefully, fully acknowledging the dynamic relationship between science and religion. While some of these applications are still far off, the potential benefits should be obvious.

This paper will review four dimensions of this area of research with a critical perspective on methodology and statistical analysis. The four dimensions as they relate to the neuroscientific study of religious and spiritual phenomena are: 1) Appropriate measures and definitions; 2) Subject selection and comparison groups; 3) Study design and biostatistics; and 4) Theological and epistemological implications.

1. Measurement and Definition of Spirituality and Religiousness

One of the most important issues related to the measurement of religious and spiritual phenomena has to do with correlating subjective and objective measures. For example, if a particular type of meditation reduces blood pressure or is associated with changes in cerebral metabolism, it is critical to know what was actually experienced by the individual.

Subjective Measures

In some sense, the most important measures of religious and spiritual phenomena are those that pertain to the subjective nature of the experience. When any person has a religious or spiritual experience, they can usually try to describe it in terms of various cognitive, behavior, and emotional parameters. Furthermore, a person will usually define the experience as "spiritual" which distinguishes the experience from others which are regarded as "non-spiritual". The issue of measuring the subjective nature of these phenomena is akin to opening the mysterious "black box" in which something is happening, but it is not immediately observable by an outside investigator. The problem becomes more difficult when trying to compare experiences across individuals and across cultures. A spiritual experience for a Jew may be vastly different than a spiritual experience for a Hindu. Furthermore, there is likely to be a continuum of experiences ranging from barely perceptible to absolutely mystical (d'Aquili and Newberg, 1993). The question for any researcher is how to qualitatively ascertain the subjective component of such experiences. Is there a way to quantify and compare these subjective feelings and thoughts individuals have regarding their spiritual experiences? It is difficult to develop adequate scales to measure spirituality and religiousness. Many existing scales are difficult to find in the literature especially when they are reported in non-scientific journals that are not typically cited or referenced in literature reviews (Larson, Swyers, and McCullough, 1998).

A number of attempts have been reported in the literature to develop a self-reporting scale that measures the subjective nature of a particular religious or spiritual phenomenon. The book, Measures of Religiosity (Hill and Hood, 1999), provides fertile grounds for various scales and questionnaires that assess everything from a person's feeling of commitment to awe to hope to the direct apprehension of God. Some have been assessed for validity and reliability, which is critical if these scales are to have any use in future research studies. Testing the validity implies that the results return information about what the scale is supposed to measure (Patten, 2000). For example, a valid scale of a feeling of hopefulness would ask questions regarding the amount of hope a person has. If this scale did not address hope, but rather happy emotional responses, it would not be a valid measure of hope. Reliability assesses whether the scale when given to the same person at different time points yields roughly the same results (Patten, 2000). While it is important to assess the reliability and validity of scales, this is particularly problematic with regard to religious and spiritual phenomena. The reason for this difficulty is the problem with defining these terms. If someone defines spiritual as a feeling of "awe" and another defines it as a feeling of "oneness", what types of questions should be used to assess spirituality? A questionnaire that asks about feelings of awe might not truly be measuring spirituality and therefore, until clear and operational definitions of spirituality and religiousness can be determined, there will always be the potential problem of developing valid scales. Reliability is also a problem since spirituality and religiousness can be very consistent or widely variable within an individual. Thus, they might subjectively feel differently at different time points and therefore, the reliability of any scale with the intention to measure spirituality is always problematic.

Another problem with individual scales is whether they are useful across traditions and cultures. For example, many of the scales that are referenced in Measures of Religiosity are Christian-based, and therefore, may not be useful for evaluating Jewish or Buddhist perspectives. Fortunately, there are other scales which either have a more universal quality or at least can be modified to accommodate other perspectives. However, this might bring into question the validity and reliability of such scales in different contexts.

There is another interesting problem with scales that attempt to measure the subjective nature of spiritual or religious phenomena. This arises from the fact that most scales of spirituality and religiousness require the individual to respond in terms of psychological, affective, or cognitive processes. Thus, questions are phrased: How did it make you feel? What sensory experiences did you have? What did you think about your experience? On one hand, such measures are very valuable to individuals interested in exploring the neural correlates of such experiences because psychological, affective, and cognitive elements can usually be related to specific brain structures or function. However, the problem with phrasing questions in this way is that one never actually escapes the neurocognitive perspective to get at something that might be "truly" spiritual. It might be suggested that the only way in which an investigator can reach something which is truly spiritual would be through a process of elimination in which all other factors – i.e. cognitive, emotional, sensory – are eliminated through the analysis, leaving only the spiritual components of the experience. In other words, the most interesting result from a brain scan of someone in prayer would be to find no significant change in the brain during the time that the individual has the most profound spiritual experience.

As described above, part of the problem with developing adequate measures is ensuring that they measure what they claim to measure. A subjective scale designed to measure the degree of an individual's religiosity needs to focus on the things which make someone religious. However, this first requires a clear definition of religiousness and spirituality. Furthermore, these definitions must be operationalized so that any measure or study can have a firm enough grasp to actually measure something (Koenig, 1998, Koenig, McCullough, and Larson, 2001). To that end, it is important to avoid narrow definitions that might impede research and also to avoid broad definitions that cannot be measured. For example, definitions of religion that pertain to a single God would eliminate almost two billion Hindu and Buddhist individuals from analysis. On the other hand, a definition of religiousness that is too broad might end up including many bizarre experiences and practices such as cults or devil worship.

One final issue, which is related to problems with definitions, is that there are so many approaches to religious and spiritual phenomena that it is often difficult to generalize from one study to another. Some scholars have pointed out that one type of meditation practice may be very different from other types, or one type of experience might be substantially different that other types (Andresen, 2000; Andresen and Forman, 2000). It is certainly critical to ensure that any study clearly states the specific practices, sub-practices, and traditions involved. Furthermore, changes in the brain associated with one type of meditative practice may not be specifically related to a different type of practice. Of course, the dynamic nature of this body of research may also provide new ways of categorizing certain practices or experiences so that one can address the question regarding whether different types of meditation truly are different, or are only experienced to be different.

O*bjective Measures of Spirituality*

Objective measures of religious and spiritual phenomena that pertain to the neurosciences include a variety of physiological and neurophysiological measures. Recent advances in fields such as psychoneuroendocrinology and psychoneuroimmunology address the important interrelationship between the brain and body. Any thoughts or feelings perceived in the brain ultimately have effects on the functions throughout the body. While this can complicate measures as well as introduce confounding factors, this integrated approach allows for a more thorough analysis of religious and spiritual phenomena (Newberg and Iversen, 2003). Several

types of measures which have already been reported in the literature include measures of autonomic nervous system activity. These are the most common approaches to specific religious and spiritual practices such as meditation or prayer. A number of studies have revealed changes in blood pressure and heart rate associated with such practices (Sudsuang, Chentanez, and Veluvan, 1991; Jevning, Wallace, and Beidebach, 1992; Koenig, McCullough, and Larson, 2001). It is interesting that the actual changes may be quite complex, involving both a relaxation as well as an arousal response. Early work by Gellhorn and Kiely (1972) developed a model of the physiological processes involved in meditation based almost exclusively on autonomic nervous system (ANS) activity, which while somewhat limited, indicated the importance of the ANS during such experiences. These authors suggested that intense stimulation of either the sympathetic or parasympathetic system, if continued, could ultimately result in simultaneous discharge of both systems (what might be considered a "breakthrough" of the other system). Several studies have demonstrated predominant parasympathetic activity during meditation associated with decreased heart rate and blood pressure, decreased respiratory rate, and decreased oxygen metabolism (Sudsuang, Chentanez, and Veluvan, 1991; Jevning, Wallace, and Beidebach, 1992; Travis, 2001). However, a recent study of two separate meditative techniques suggested a mutual activation of parasympathetic and sympathetic systems by demonstrating an increase in the variability of heart rate during meditation (Peng, Mietus, Liu, et al., 1999). The increased variation in heart rate was hypothesized to reflect activation of both arms of the autonomic nervous system. This notion also fits the characteristic description of meditative states in which there is a sense of overwhelming calmness as well as significant alertness. Also, the notion of mutual activation of both arms of the ANS is consistent with recent developments in the study of autonomic interactions (Hugdahl, 1996).

Measures of hormone and immune function have more recently been explored especially as an adjunct measure to various clinical outcomes (O'Halloran, Jevning, Wilson, et al., 1985; Walton, Pugh, Gelderloos, and Macrae, 1995; Tooley, Armstrong, Norman, and Sali, 2000; Infante, Torres-Avisbal, and Pinel, et al., 2001). Thus, if a hypothetical study showed that the practice of meditation results in reductions in cancer rates, then it might be valuable to measure the immunological and hormonal status of the individuals to determine the physiological basis of the effect. Certain cancers are related to abnormalities in immune (i.e. leukemia or lymphoma) or hormonal function (i.e. breast and prostate cancer). It is also important to note that alterations in various hormones and immune functions may be related to specific changes in brain function. Further, this interaction can be bidirectional. Thus, certain brain states may enhance hormonal status, but these hormonal states may in turn affect brain function. This can particularly be observed in women with premenstrual syndrome, but there are other circumstances in which various neurohormones can alter emotional, cognitive, and behavioral states.

Neurophysiological changes associated with religious and spiritual states can be obtained through a number of techniques that each have their own advantages and disadvantages. In general, the primary requirement is that the methodology evaluates functional changes in the brain. However, there are many ways of measuring such functional changes. Early studies of meditation practices made substantial use of electroencephalography (EEG) that measures electrical activity in the brain (Banquet, 1973; Hirai, 1974; Hebert, Lehmann, 1977; Corby, Roth, Zarcone, Kopell, 1978). EEG is valuable because it is relatively non-invasive and has very good temporal resolution. In other words, the instant that an individual achieves a certain state, the EEG should change accordingly. For this reason, it has continued to be useful in the evaluation of specific meditation states (Lehmann et al., 2001; Aftanas and Golocheikine, 2002; Travis and

Arenander, 2004). The major problem with EEG is that spatial resolution is very low so that any change can only be localized over very broad areas of the brain. Another problem is that analysis can be difficult because of the extensive amount of recordings that are made during any session. However, EEG may be particularly valuable to include in studies employing functional imaging techniques since the EEG may help to signal certain states, or at the very least, ensure that the individual being studied has not fallen asleep.

Functional neuroimaging studies of religious and spiritual phenomena might become one of the most important techniques since the results have physiological, clinical, and potentially philosophical relevance to the issues related to such phenomena. To date, brain imaging studies have utilized positron emission tomography (PET), single photon emission computed tomography (SPECT), and functional magnetic resonance imaging (fMRI). In general, such techniques can measure functional changes in the brain in pathological conditions, in response to pharmacological interventions, and during various activation states. Activation states have included sensory stimulation (i.e. vision, auditory, etc.), motor function and coordination, language, and higher cognitive functions (i.e. concentration) (Newberg and Alavi, 1996). The changes that can be measured include more general physiological processes such as cerebral blood flow and metabolism, in addition to many aspects of the neurotransmitter systems. For example, the serotonin, dopamine, opiate, benzodiazepine, glutamate, and acetylcholine systems have all been evaluated in a number of brain states (Newberg and Alavi, 2003; Warwick, 2004; Kennedy and Zubieta, 2004).

While functional neuroimaging studies have contributed greatly to the understanding of the human brain, they each have their own advantages and limitations with respect to evaluating religious and spiritual phenomena. Functional MRI primarily measures changes in cerebral blood flow. In general, this is a valid method for measuring cerebral activity since a brain region that is activated during a specific task will experience a concomitant increase in blood flow. This coupling of blood flow and activity provides a method for observing which parts of the brain have increased activity (increased blood flow) and decreased activity (decreased blood flow). Functional MRI has several advantages. Functional MRI has very good spatial resolution and can be coregistered with an anatomical MRI scan that can be obtained in the same imaging session. This allows for a very accurate determination of the specific areas of the brain that are activated. Functional MRI also has very good temporal resolution so that many images can be obtained over very short periods of time, as short as a second. Thus, if a subject was asked to perform 10 different prayers sequentially while in the MRI, the differences in blood flow could be detected in each of those 10 prayer states. Finally, fMRI does not involve any radioactive exposure. The disadvantages are that images must be obtained while the subject is in the scanner and the scanner can make up to 100 decibels of noise. This can be very distracting when individual are performing various spiritual practices such as meditation or prayer. However, several investigators have successfully utilized fMRI and have performed the study by having subjects practice their meditation technique at home while listening to a tape of the fMRI noise so that they become acclimated to the environment (Lazar, Bush, Gollub, Fricchione, Khalsa, Benson, 2000). The MRI noise can also affect brain activity, particularly in the auditory cortex. Functional MRI also relies on a tight coupling between cerebral blood flow and actual brain activity, which while a reasonable assumption, is not true in all cases. Well known examples in which brain activity and blood flow are not coupled include stroke, head injury, and pharmacological interventions (Newberg and Alavi, 2003). However, a detailed evaluation of

this coupling in all brain states has not been performed. One final disadvantage is that at the present moment, fMRI cannot be used to evaluate individual neurotransmitter systems.

PET and SPECT imaging also have advantages and disadvantages for studying religious and spiritual phenomena. The advantages include relatively good spatial resolution for PET (comparable to fMRI) and slightly worse for SPECT imaging. PET and SPECT images can also be coregistered with anatomical MRI, but this must be obtained during a separate session and therefore, matching the scans is more difficult. PET and SPECT both require the injection of a radioactive tracer so radioactivity is involved, although usually this is fairly low. Depending on the radioactive tracer used, a variety of functional parameters can be measured including blood flow, metabolism (which more accurately depicts cerebral activity), and many different neurotransmitter components. The ability to measure these neurotransmitter systems is unique to PET and SPECT imaging. Such tracers can measure either state or trait responses. It should also be mentioned that some of the more common radioactive materials such as fluorodeoxyglucose (that measures glucose metabolism) can be injected through an existing intravenous catheter when the subject is not in the scanner. This allows for a more conducive environment for performing practices such as meditation and prayer. This tracer becomes "locked" in the brain during the injection period and the person can then be scanned after the person has completed their practice, but still measure changes associated with the practice (Herzog, 1990-1991; Newberg, Alavi, Baime, Pourdehnad, Santanna, and d'Aquili, 2001). A major drawback to PET and SPECT imaging, in addition to the radioactive exposure, is that these techniques have generally poor temporal resolution. Depending on the tracer, the temporal resolution can be as good as several minutes and as bad as several hours or even days. PET or SPECT would be very difficult to use in order to study 10 different prayer states in the same session. However, 2 or 3 states might be measured in the same imaging session if the appropriate radiopharmaceutical is used (Lou, Kjaer, Friberg, Wildschiodtz, Holm, Nowak, 1999). The result of this discussion is that depending on the goals of the study, various neuroimaging techniques might be better or worse.

There are other more global problems that affect the ability to interpret the results of all functional imaging studies. The most important of which is how to be certain what is actually being measured physiologically and how it compares to various subjective experiences. There are already potential problems addressing what a particular scan finding means in terms of the actual activity state of the brain. For example, it is not clear what will be observed if there is increased activity in a group of inhibitory neurons. Would that result in increased or decreased cerebral activity as measured by PET or fMRI? The bigger problem is trying to compare the physiological changes observed to the subjective state. With regard to religious and spiritual experience, it is not possible to intervene at some "peak" experience to ask the person what they are feeling. Therefore, if a person undergoes fMRI during a meditation session and they have a peak experience, how will the researcher know which scan findings relates to it? In addition, there are typically a number of changes in the brain with varying degrees of strength. It is not clear what degree of change should be considered a relevant change (i.e. 10% or 20%, etc.). From a statistical perspective, analyzing images has a number of problems including how to compare images across subjects and conditions and how to take into account the problems of multiple comparisons both in terms of activation states and also in terms of individual brain regions. A program called statistical parametric mapping (SPM) has been developed which can be used to evaluate various images and works by normalizing the images, coregistering the images and then analyzing them pixel by pixel for significant changes (Friston, Holme, Worsley,

Poline, Frith, and Frackowiak, 1995). This is a very conservative statistical approach because of the problem with multiple comparisons and therefore subtle changes may be missed. Of course, the question still arises as to whether changes observed which are not significant in SPM are still clinically relevant. Furthermore, in the study of religious and spiritual states, it may be important to evaluate subjects on an individual basis since such states may be highly variable phenomenologically across subjects.

In spite of these limitations, neuroimaging studies have been successfully utilized to evaluate specific spiritual and meditative practices. There are currently six known studies which have spanned the different neuroimaging techniques (Herzog, 1990-1991; Lou, Kjaer, Friberg, Wildschiodtz, Holm, Nowak, 1999; Lazar, Bush, Gollub, Fricchione, Khalsa, Benson, 2000; Newberg, Alavi, Baime, Pourdehnad, Santanna, and d'Aquili, 2001; Kjaer, Bertelsen, Piccini, Brooks, Alving, and Lou, 2002; Newberg, Pourdehnad, Alavi, d'Aquili, 2003). Interestingly, there appears to be some coherence of their findings with the frontal lobes, parietal lobes, thalamus, and limbic system appearing to be related in network associated with such practices. It may be that the variety of different types of practices activate a network of brain structures in relatively similar ways. It is also interesting that there do seem to be some differences that correlate well with the variations among the approaches. One study also measured changes in the dopamine system and found increased activity during meditation related practices (Kjaer, Bertelsen, Piccini, Brooks, Alving, and Lou, 2002). Thus, the level of complexity of our understanding continues to improve as more studies are performed. Future studies will certainly be necessary to more thoroughly evaluate the neurophysiological changes that occur in the brain during various religious and spiritual phenomena.

2. Subject Selection and Comparison Groups

Another interesting methodological issue in the study of religious and spiritual phenomena is to determine who are the most appropriate subjects to study and who should represent the comparison group(s). The issue of whom to study with regard to religious and spiritual phenomena depends somewhat on the definition of the phenomena. Obviously, if a researcher wanted to evaluate physiological changes during meditation, there would be thousands of different possible groups to consider studying. It is important to determine which elements of a particular practice or experience are of most interest. The more specific a researcher wants to be in terms of the phenomena, the more focused will be the subject group. For example, if a researcher wanted to study the physiological effects of the Rosary, the group would have to consist of those individual who practice the Rosary. If the focus is on feelings of unity, there may be many different practices that could be chosen, or perhaps the study group will consist of individuals from many different backgrounds. An important issue in this regard is the level of expertise or proficiency of the individuals being studied. In the case of meditative practices, there could be varied results between novice, experienced, and master level individuals. These differences could be related to whether more novice individuals can perform the practice in a manner that is similar to their usual level of practice while under the scrutiny of the researcher. For example, the noise of an MRI scanner may result in a novice not being able to perform their practice of meditation adequately while a more experienced individual may have less of a problem with the distraction. Thus, the difference observed might be related to the fact that one of them successfully performed the practice rather true differences between the practices. It is also important to select individuals that have similar socioeconomic and health

backgrounds. If Franciscan nuns are less likely to smoke, then their brain scans might differ from a group of other individuals who do smoke.

The other major issue in terms of subject selection relates to the comparison or control groups. One possibility, which is frequently employed in functional neuroimaging studies is that the individual acts as their own comparison. Studies of various meditative practices typically compare the meditation state to the subject's own baseline waking state. Others have suggested that a more appropriate comparison would be a state in which they are doing a task that is similar, but has no specific spiritual meaning. For example, one study explored whether different mantras (some spiritual some not) have different effects on the brain electrical activity during meditation (Telles, Nagarathna, and Nagendra, 1998). Another issue with regard to using subjects as their own comparison involves excluding other factors that are part of the practice. Thus, a practice that involves burning incense would be better to compare to a baseline state in which incense is also used. Otherwise, the primary change observed would be in the olfactory regions of the brain and may have nothing to do with the spiritual practice. Similarly, if a practice requires the eyes to be open (i.e. reading prayers), then the baseline state should have the subject with their eyes open, or possibly even reading non-religious texts. Some studies have looked at such differences and have found distinctions in cerebral activity depending on whether a subject was reading a religious or non-religious text (Azari, 2001). Other types of practices might also be used as comparisons including artistic and creative practices, athletic events, or cognitive and visuo-spatial tasks. Comparison groups could be other practitioners in the same tradition, but with different levels of expertise or practitioners in other traditions in which similar practices are performed. These groups might help to determine longitudinal effects of various spiritual practices, but factors such as age and health might interfere with the interpretation of such studies.

Placebo groups are another important problem with the study of religious and spiritual phenomena. It is not clear what a placebo would represent in many cases since most people who are spiritual know whether or not they are actually performing their spiritual practice. Placebo groups in this case more likely will represent other tasks that resemble the spiritual one, but are lacking the specific spiritual content. Thus if reading a prayer is going to be studied, then reading a non-religious text would represent a reasonable comparison group.

3. Study Design and Biostatistical Analysis

Based on the above review of the existing literature and the proposed operational definition of spiritual experience, there are at least seven neuroscientific paradigms which can readily contribute to the initial operationalization of spiritual experience (Larson, Swyers, and McCullough, 1998). These seven paradigms include: 1) the neurophysiology of spiritual interventions, 2) spiritual interventions associated with psychopharmacological agents, 3) drug-induced spiritual experiences, 4) neuropathologic and psychopathologic spiritual experiences, 5) spiritual experiential development in infants, children and adolescents, and 6) physical and psychological therapeutic interventions. After these study designs are considered, the biostatistical issues with such studies can be reviewed.

The Neurophysiology of Spiritual Interventions

The first paradigm involves an experimental spiritual intervention such as prayer or meditation with concomitant measures of a psychological- and spiritual- dependent evaluation.

This will help to define and delineate the nature of the spiritual intervention itself. These psychological and spiritual measures can then be compared to simultaneously derived neurobiological parameters, such as electroencephalographic activity, cerebral blood flow, cerebral metabolism, and neurotransmitter activity. Such measures can be performed with state of the art imaging techniques including positron emission tomography (PET), single photon emission computed tomography (SPECT) and magnetic resonance imaging (MRI). Body physiological scalar parameters such as blood pressure, body temperature, heart rate, and galvanic skin responses (that measures autonomic nervous systems activity) can also be measured. Other body physiological parameters such as immunological assessments, hormonal concentrations, and autonomic activity should also be included to complete a thorough analysis of the effects of spiritual interventions.

Altering Spiritual Interventions

The second existing paradigm that might be employed to investigate spiritual experience from a neuroscientific approach uses pharmacological agents or other interventions in an attempt to alter spiritual interventions. Using this paradigm, a previously measured spiritual practice will be compared to the same practice with the addition of some intervention. For example, studies might attempt to show the effects of an opiate antagonist on the strength of the subjective experience of meditation or prayer. Preliminary studies (on one or a few subjects) of this type have shown no effect on EEG patterns during meditation when subjects were given either an opiate or benzodiazepine antagonist (Sim and Tsoi, 1992). The effects of transcranial magnetic stimulation, other pharmacological agents, or even surgical procedures (performed for other purposes) could be evaluated. However, it is clear that more extensive studies measuring a number of neurophysiological parameters are required. Other agonists and antagonists may be utilized to determine their ability to augment or diminish spiritual experiences. In addition, the exploration of various pharmacological agents on spiritual interventions may help to delineate the role of different neurotransmitter systems. Such studies also offer the possibility of measuring dose responses in terms of spiritual interventions.

Drug-Induced Spiritual Experiences

A third paradigm that might be employed utilizes those people whose use of hallucinogenic agents has resulted in intensive spiritual experiences. Since it has long been observed that drugs such as opiates, LSD, and stimulants can sometimes induce spiritual experiences, careful studies of the types and characteristics of drug-induced spiritual experiences, perhaps utilizing modern imaging techniques, may help elucidate which neurobiological mechanism are involved in more "naturally derived" spiritual experiences. Some studies related to the use of such hallucinogenic agents have already been performed (Vollenweider, Leenders, Scharfetter, Maguire, Stadelmann, Angst, 1997; Vollenweider, Vontobel, Hell, Leenders, 1999; Vollenweider, Vontobel, Oye, Hell, Leenders, 2000), but a more extensive study of such agents, particularly in relation to religious and spiritual experiences is required. Comparing this paradigm to naturally occurring spiritual phenomena may allow for a better distinction of pathologic and non-pathologic spiritual experiences. There are obvious ethical and legal considerations with studies such as these (although studies outside of the United States may be more possible). However, subjects who have had pharmacologically induced spiritual experiences can be studied using radioactive analogues of such agents as a means of determining the concentration of receptors and their agonists. Another related approach would

be to study the effects of drug withdrawal on spiritual experience. However, there are no reports in the literature of such findings.

Neuropathologic and Psychopathologic Spiritual Experiences

A fourth paradigm would utilize patients with various known neuropathologic and psychopathologic conditions. Neurological conditions including seizure disorders, particularly in the temporal lobes, brain tumors, and stroke, have been associated with spiritual experiences or alterations in religious beliefs. For example, temporal lobe epilepsy has been associated with hyperreligiosity and religious conversions (Bear, 1979; Bear and Fedio, 1977). Psychiatric disorders such as schizophrenia and mania also have been associated with spiritual experiences and religious conversions. Delineating the type of pathology and the location of that pathology will aid in determining the neurobiological substrate of spiritual experience. Thus, neuropsychiatric disorders can be an effective tool for the neuroscience of spiritual experience.

Research on pathological conditions has classically been used to elucidate the normal functions of biological systems. Spiritual experiences in psychiatric and neurological disorders may be central to the identification of largely nascent neurobiological systems that subserve "normal" spiritual experience. This presents a crucial distinction to the historic psychiatric implication that spiritual experience is an expression of psycho- or neuro- pathology. This provides a framework in which normal spiritual experience can occur in pathological and normal conditions and pathologic spiritual episodes might occur in individuals with or without psychopathological disorders. However, care must be taken to avoid referring to spiritual experience only in pathological terms or associated with pathological conditions as well as not reducing spiritual experiences only to neurophysiological mechanisms.

Spiritual Experiential Development

There has been a fairly extensive literature regarding the developmental aspects of religion and spiritual experience (Fowler, 1981; Tamminen, 1994; Oser, 1991). These reports consider the overall development of spiritual experience from infancy through adolescence and into adulthood. There is also consideration of the necessary neurocognitive developments for spiritual experience to arise. For example, a more primitive form of undifferentiated faith may occur in infancy while the more complex aspects of spiritual experience which include cognitive, cultural, and affective components usually requires growth into adulthood (Fowler, 1981). Most of these analyses of spiritual experiential development are grounded in psychology. However, neuroscience may be able to utilize these findings and compare them to the development of various brain structures and neurocognitive processes. This may help elucidate which brain structures and functions are required for various components of spiritual experience. The developmental approach can also be viewed from the end of life perspective. For example, alterations in spiritual functions may be associated with diffuse neuropathological conditions (e.g. dementia). Furthermore, it may be useful to study alteration in spiritual functions that are associated with decrements in neurocognitive functions as well as decrements in physical health.

Physical and Psychological Therapeutic Interventions

There are a large number of ongoing studies which have explored the therapeutic effects of meditation, stress management, prayer, and other related interventions for various psychological and physical disorders including anxiety disorders, hypertension, coronary artery disease, cancer, and the human immunodeficiency virus (Kabat-Zinn, 1992; Carson, 1993; Levin

1989, 1994; Miller 1995; Leserman 1989; Zamarra 1996; Massion 1995; Schneider 1995). While these studies focus on the effects of the intervention on various disease parameters, it may be possible to "piggy-back" onto these studies to include measures of spiritual experience and well-being. Utilizing measurement scales already available in the literature, it may be possible to determine the relationship of spiritual experiences and well-being to the intervention as well as to the progression of the disorder. Performing high quality studies is essential to demonstrating the relationship between spirituality and health especially in light of the various criticisms that have been raised regarding methodological issues with these early studies (Sloan, Bagiella, and Powell, 1999; Sloan and Bagiella, 2002).

Statistical Analysis Issues

In terms of statistical analysis, there are several issues that arise in the study of religious and spiritual phenomena. To begin with, religious and spiritual phenomena are frequently very complex with many different components. As mentioned above, these components can be both subjective and objective. In order to account for this variety of components, there are frequently a number of variables that must be factored into the statistical analysis. Thus, simple statistical comparisons will frequently oversimplify the findings and may miss important covariates that may have significant contributions to the findings. Every effort should be made to perform statistical analyses in studies of religious and spiritual phenomena with the same rigor and complexity as other biomedical studies. To this end, it is imperative that well qualified statisticians are utilized to evaluate data from these studies in order to ensure the highest quality of such research.

Another problem that may be somewhat unique to religious phenomena is the interindividual differences that may be beneficial to evaluate. For example, in our research study of Tibetan Buddhist meditators, we asked each participant to practice the same type of meditation for the same amount of time. In this way, the data were easier to pool for group analysis. However, we may have missed important interindividual differences related to the strength and depth of the meditation practice, the specific experiences an individual may have had, and whatever unique techniques each person may utilize as part of their practice. Unfortunately, statistical analysis becomes more limited in evaluating interindividual differences, especially when the focus is on physiological measures in the brain or body. Future development of analyses that can better explore such interindividual differences could be highly beneficial to this field.

4. Theological and Epistemological Implications

One of the most ancient problems of philosophy is, "How do we know that the external world corresponds, at least partially, to our mental representation of it?" The question of what is "really real" has been considered, with various answers, since the time of the presocratic Greek philosophers in the West. Preoccupation with this question is even older in Eastern religio-philosophical traditions. In considering the neuroscientific approach to religious and spiritual phenomena, one can ponder whether epistemological issues can actually be addressed.

With regard to this issue, a number of researchers claim that because there is a neurobiological correlate of a religious phenomenon, there is nothing more to that phenomenon. While this interpretation may ultimately be accurate, that a neurobiological correlate exists does not specifically refer to the causal mechanism of such phenomena. In other words, if the brain activity changes during a mystical communion with God, it is not clear whether the brain activity

caused that experience or responded to that experience. Even situations in which certain religious states are induced by pharmacological agents does not necessarily detract from the spiritual nature of these states. Shamanic practices in which various substances are ingested to aid in the spiritual journey are not viewed as less real or less spiritual because of the use of these substances. On the other hand, use of such substances alone do not typically result in profound religious experiences. It is clear that the specific context in which various practices and experiences arise is also crucial to the spiritual nature of those phenomena.

However, in reconsidering the epistemological question from a neuroscientific perspective, a term sometimes referred to as "neuroepistemology", how reality is experienced in the brain, results in a complex paradox (Newberg, d'Aquili, and Rause, 2001). For example, the three most common criteria given for judging what is real are:

1. The subjective vivid sense of reality.
2. Duration through time.
3. Agreement intersubjectively as to what is real.

Each of these can be related to specific brain functions. But, it may be demonstrated that all three of these criteria determining what is real can be reduced to #1 above -- the vivid sense of reality. For example, the sense of duration through time depends on the structuring of time in baseline reality. It appears that the ability to have a sense of time, or more properly duration, is structured by the brain. Alteration of the function of parts of the brain that subserve temporal ordering, for any reason, results in a significant distortion of the perception of time in a number of ways. Most dramatically, during various spiritual practices and states, there is no sense of time or duration while the person is in that state. It becomes obvious that time and duration are not absolutes, and derive their perceived qualities from brain structuring. Hence, it begs the question to derive the reality of baseline reality from one of the *qualia,* in this case time, which is itself structured by baseline reality (the brain). This same critique applies to any appeal for the reality of objects which depend on characteristics of baseline reality the perception of which is known to be structured by the brain. The third criterion for the reality of entities, i.e. intersubjective validation, again arises from begging the question. The "subjects" who agree or disagree about entities being real are themselves only images or representations within the sensori-cognitive field of the analyzing subject-philosopher. Thus, it is unfortunately true that any person analyzing his or her own experience must start out, at least, as a naive solipsist.

These analyses could continue ad infinitum. Suffice it to say that we are satisfied that each and every criterion of the reality of entities collapses into the first, i.e. the vivid sense of reality. If we are forced to conclude that reality is ultimately reducible to the vivid sense of reality, then what are we to make of religious and spiritual states that appear to the experiencing subject as more real than baseline reality, even when they are recalled from within baseline reality. If we take baseline reality as our point of reference, it seems that there are some states the reality that appear to be inferior to baseline reality and some states the reality that appear to be superior to that of baseline reality when these states are recalled in baseline reality? And this is the crucial point. These different experiences of reality appear more real than baseline reality *when recalled from baseline reality.* Thus, individuals almost always refer to dreams as inferior to baseline reality when they are recalled and discussed within baseline reality. The same is true of psychotic hallucinations -after they are cured by phenothiazines or other psychotropic medications. A person having emerged from such a psychotic state will recall it as psychotic.

The same cannot be said, however, of many religious and spiritual states which appear to be "more real" than baseline reality and are vividly described as such by experiencers after they return to baseline reality. This is true of a number of such states including absolute unitary states, (Newberg, d'Aquili, and Rause, 2001), Cosmic Consciousness as described by Bucke (1961), certain trance states, hyperlucid visions (usually of religious figures, religious symbols, and dead persons), and near death experiences (Newberg and d'Aquili, 1994). So real do these experiences appear when recalled in baseline reality that they often alter the way the experiencers live their lives. Studies have actually been performed on this topic with near death experiencers. Those who have had the core experience clearly behave more altruistically, more kindly, and with greater compassion towards other human beings than they showed before the experience (Ring, 1980). Furthermore, there is a marked tendency for near death experiencers not to fear death. And these beneficial changes do not persist for just a short period of time after the near death experience, but seem to persist for many years or even a lifetime.

Again, if it is true that all of the proposed criteria by which reality is judged to be real can be reduced, in the last analysis, to the vivid sense of reality, then we have no choice but to conclude that in some sense, these states, and especially absolute unitary states or pure consciousness, are, in fact, more real than the baseline reality of our everyday lives. And the word "real" here is not used in a poetic or metaphorical sense. It is used in the same sense as in the utterance "this rock or this table is real." Suffice it to say that, when one approaches questions of reality from a neuroscientific perspective, "reality" becomes a very slippery concept, often manifesting itself in profoundly counterintuitive ways to the scientist, philosopher, or mystic.

Conclusion

While the neuroscientific evaluation of religious and spiritual phenomena has advanced considerably since some of the initial studies that were performed over 30 years ago, this field of research is still in its early stages. There are many unique methodological issues that face this field in addition to the potentially more problematic barriers of funding and academic stature. However, pursuit of such projects may ultimately pay large dividends both for science and religion. From the religious perspective, the results of such studies may help towards a better understanding of the human experience of religion. These studies enhance human knowledge of how spiritual and religious pursuits affect the mind, brain, body, and behavior. From the scientific perspective, such research may shed new light on the complex workings of the human brain as well as the relationship between brain states and body physiology. Finally, addressing methodological and statistical issues can enhance both fields since such issues may result in improved scientific and statistical techniques and also contribute to theological and philosophical dialogue. Overall, this integrated field of neuroscience and religion should be an important area of scholarship for the 21st century and beyond.

References

Aftanas LI, Golocheikine SA. Non-linear dynamic complexity of the human EEG during meditation. Neurosci Lett. 2002 Sep 20;330(2):143-6.

Andresen J, Forman RKC. Methodological pluralism in the study of religion - How the study of consciousness and mapping spiritual experiences can reshape religious methodology. Journal of Consciousness Studies 7 (11-12): 7-14 2000.

Andresen J. Meditation meets behavioural medicine - The story of experimental research on meditation. Journal of Consciousness Studies 7 (11-12): 17-73 2000.

Azari NP, Nickel J, Wunderlich G, Niedeggen M, Hefter H, Tellmann L, Herzog H, Stoerig P, Birnbacher D, Seitz RJ. Neural correlates of religious experience. Eur J Neurosci. 2001 Apr;13(8):1649-52.

Banquet JP. Spectral analysis of the EEG in meditation. Electroencephalogr Clin Neurophysiol. 1973 Aug;35(2):143-51.

Bear DM and Fedio P. (1977). Quantitative analysis of interictal behavior in temporal lobe epilepsy. *Arch Neurol* 34:454-467.

Bear DM. (1979). Temporal lobe epilepsy -- A syndrome of sensory-limbic hyperconnection. *Cortex* 15:357-384.

Bucke, R.M. (1961). *Cosmic Consciousness*, Secaucus, NJ: Citadel Press.

Carson VB. (1993). Prayer, meditation, exercise, and special diets: Behaviors of the hardy person with HIV/AIDS. *JANAC* 4:18-28.

Corby, J.C. Roth WT, Zarcone VP Jr, Kopell BS. (1978). Psychophysiological correlates of the practice of tantric yoga meditation. Archives of General Psychiatry, 35, 571-577.

d'Aquili EG, Newberg AB. (1993). Religious and mystical states: A neuropsychological model. *Zygon* 28:177-99.

Fowler, J.W. (1981). *Stages of faith*. San Francisco, Harper Collins Publishers.

Friston KJ, Holmes AP, Worsley KJ, Poline JP, Frith CD, Frackowiak RSJ. 1995. Statistical parametric maps in functional imaging: a general linear approach. Human Brain Mapping 2, 189-210.

Gellhorn E., Kiely W.F. Mystical states of consciousness: Neurophysiological and clinical aspects. *J Nerv Mental Dis* 1972; 154, 399-405.

Hebert R, Lehmann D. Theta bursts: an EEG pattern in normal subjects practising the transcendental meditation technique. Electroencephalogr Clin Neurophysiol. 1977;42(3), 397-405.

Herzog H, Lele VR, Kuwert T, Langen, K-J, Kops ER, Feinendegen LE. Changed pattern of regional glucose metabolism during Yoga meditative relaxation. Neuropsychobiology 1990-1991;23, 182-187

Hill, P.C., Hood, R.W. (1999). Measures of Religiosity. Religious Education Press.

Hirai, T. (1974). Psychophysiology of Zen. Tokyo: Igaku Shoin.

Hugdahl K., Cognitive influences on human autonomic nervous system function. *Curr Opin Neurobiol* 1996; 6, 252-258.

Infante JR, Torres-Avisbal M, Pinel P, Vallejo JA, Peran F, Gonzalez F, Contreras P, Pacheco C, Roldan A, Latre JM. Catecholamine levels in practitioners of the transcendental meditation technique. *Physiol Behav* 2001; 72(1-2),141-6.

Jevning R, Wallace RK, Beidebach M. (1992). The physiology of meditation: A review. A wakeful hypometabolic integrated response. *Neurosci Biobehav Rev* 16:415-424.

Kabat-Zinn J. Massion AO. Kristeller J. Peterson LG. Fletcher KE. Pbert L. Lenderking WR. Santorelli SF. (1992). Effectiveness of a meditation-based stress reduction program in the treatment of anxiety disorders. *American Journal of Psychiatry* 149:936-43.

Kennedy SE, Zubieta JK. Neuroreceptor imaging of stress and mood disorders.CNS Spectr. 2004 Apr;9(4):292-301.

Kjaer TW, Bertelsen C, Piccini P, Brooks D, Alving J, Lou HC. Increased dopamine tone during meditation-induced change of consciousness. Brain Res Cogn Brain Res. 2002 Apr;13(2):255-9.

Koenig H.G., McCullough, M.E., Larson, D. B. (editors). (2001). Handbook of religion and health. New York: Oxford University Press.

Koenig, H.G. (editor). (1998). Handbook of religion and mental health. San Diego: Academic Press.

Larson DB, Swyers JP, and McCullough ME (editors). (1998). *Scientific Research On Spirituality and Health: A Consensus Report.* Washington DC: National Insitute for Healthcare Research.

Lazar SW, Bush G, Gollub RL, Fricchione GL, Khalsa G, Benson H. Functional brain mapping of the relaxation response and meditation. Neuroreport. 2000 May 15;11(7):1581-5.

Lehmann D, Faber PL, Achermann P, Jeanmonod D, Gianotti LR, Pizzagalli D. Brain sources of EEG gamma frequency during volitionally meditation-induced, altered states of consciousness, and experience of the self. Psychiatry Res. 2001 Nov 30;108(2):111-21.

Leserman J, Stuart EM, Mamish ME, Benson H. (1989). The efficacy of the relaxation response in preparing for cardiac surgery. *Behavioral Medicine* 15:111-117.

Levin JS. Vanderpool HY. (1989). Is religion therapeutically significant for hypertension? *Social Science & Medicine*. 29(1):69-78.

Levin JS. (1994). Religion and health: is there an association, is it valid, and is it causal? *Social Science & Medicine* 38(11):1475-82.

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. Hum Brain Mapp. 1999;7(2):98-105.

Massion AO, Teas J, Hebert JR, Wertheimer MD, Kabat-Zinn J. (1995). Meditation, melatonin and breast/prostate cancer: Hypothesis and preliminary data. *Medical Hypothesis* 44:39-46.

Miller JJ. Fletcher K. Kabat-Zinn J. (1995) Three-year follow-up and clinical implications of a mindfulness meditation-based stress reduction intervention in the treatment of anxiety disorders. *General Hospital Psychiatry* 17(3):192-200.

Newberg A, Pourdehnad M, Alavi A, d'Aquili E. Cerebral blood flow during meditative prayer: Preliminary findings and methodological issues. *Perceptual and Motor Skills* 97: 625-630, 2003

Newberg AB, Alavi A, Baime M, Pourdehnad M, Santanna J, d'Aquili EG. The measurement of regional cerebral blood flow during the complex cognitive task of meditation: A preliminary SPECT study. *Psychiatry Research: Neuroimaging* 106: 113-122, 2001

Newberg AB, Alavi A. Role of Positron Emission Tomography in the Investigation of Neuropsychiatric Disorders. In Sandler MP, Coleman RE, Patton JA, Wackers FJT,

Gottschalk A, and Hoffer PB (editors). *Diagnostic Nuclear Medicine, Fourth Edition.* Philadelphia: Lippincott Williams & Wilkins. pp.783-819, 2003.

Newberg AB, Alavi A. The study of the neurological disorders using positron emission tomography and single photon emission computed tomography. *Journal of the Neurological Sciences* 135:91-108, 1996.

Newberg AB, d'Aquili EG, Rause VP. *Why God Won't Go Away: Brain Science and the Biology of Belief*. New York: Ballantine Publishing Group. April, 2001.

Newberg AB, d'Aquili EG. The near death experience as archetype: A model for 'prepared' neurocognitive processes. *Anthropology of Consciousness* 5:1-15, 1994.

Newberg AB, Iversen J. The neural basis of the complex mental task of meditation: Neurotransmitter and neurochemical considerations. *Medical Hypothesis* 61(2): 282-291, 2003.

O'Halloran JP, Jevning R, Wilson AF, Skowsky R, Walsh RN, Alexander C. Hormonal control in a state of decreased activation: potentiation of arginine vasopressin secretion. *Physiol Behav* 1985; 35(4):591-5.

Oser FK. (1991). The development of religious judgement. *New Directions for Child Development* 52:5-25.

Patten, M.D. (2000). Understanding Research Methods, Second Edition. Pyrczak Publishing, Los Angeles.

Peng C.K., Mietus J.E., Liu Y., et al. Exaggerates heart rate oscillations during two meditation techniques. Intern J Cardiol 1999;70:101-107.

Ring, K. (1980). *Life at Death: A Scientific Investigation of the Near-Death Experience*. New York: Quill Publishers.

Schneider RH, Staggers F, Alexander CN, et al. (1995). A randomized controlled trial of stress reduction for hypertension in older African Americans. *Hypertension* 26:820-827.

Sim MK, Tsoi WF. (1992). The effects of centrally acting drugs on the EEG correlates of meditation. *Biofeedback and Self-Regulation* 17:215-220.

Sloan RP, Bagiella E, Powell T. Religion, spirituality, and medicine. Lancet. 1999 Feb 20;353(9153):664-7.

Sloan RP, Bagiella E. Claims about religious involvement and health outcomes. Ann Behav Med. 2002 Winter;24(1):14-21.

Sudsuang R, Chentanez V, Veluvan K. (1991). Effects of Buddhist meditation on serum cortisol and total protein levels, blood pressure, pulse rate, lung volume and reaction time. *Physiol Behav* 50:543-548.

Tamminen K. (1994). Religious experiences in childhood and adolescence: A viewpoint of religious development between the ages of 7 and 20. *International Journal for the Psychology of Religion* 4:61-85.

Telles S, Nagarathna R, Nagendra HR. Autonomic changes while mentally repeating two syllables--one meaningful and the other neutral. Indian J Physiol Pharmacol. 1998 Jan;42(1):57-63.

Tooley GA, Armstrong SM, Norman TR, Sali A. Acute increases in night-time plasma melatonin levels following a period of meditation. *Biol Psychol* 2000; 53(1):69-78.

Travis F, Arenander A. EEG asymmetry and mindfulness meditation. Psychosom Med. 2004 Jan-Feb;66(1):147-8

Travis F. Autonomic and EEG patterns distinguish transcending from other experiences during Transcendental Meditation practice. *Int J Psychophysiol* 2001;42: 1-9.

Vollenweider FX, Leenders KL, Scharfetter C, Maguire P, Stadelmann O, Angst J. Positron emission tomography and fluorodeoxyglucose studies of metabolic hyperfrontality and psychopathology in the psilocybin model of psychosis. Neuropsychopharmacology. 1997 May;16(5):357-72.

Vollenweider FX, Vontobel P, Hell D, Leenders KL. 5-HT modulation of dopamine release in basal ganglia in psilocybin-induced psychosis in man--a PET study with [11C]raclopride. Neuropsychopharmacology. 1999 May;20(5):424-33.

Vollenweider FX, Vontobel P, Oye I, Hell D, Leenders KL. Effects of (S)-ketamine on striatal dopamine: a [11C]raclopride PET study of a model psychosis in humans. J Psychiatr Res. 2000 Jan-Feb;34(1):35-43.

Walton KG, Pugh ND, Gelderloos P, Macrae P. Stress reduction and preventing hypertension: preliminary support for a psychoneuroendocrine mechanism. *J Altern Complement Med* 1995; 1(3):263-83.

Warwick JM. Imaging of brain function using SPECT. Metab Brain Dis. 2004 Jun;19(1-2):113-23.

Zamarra JW, Schneider RH, Besseghini I, Robinson DK, Salerno JW. (1996). Usefulness of the transcendental meditation program in the treatment of patients with coronary artery disease. *Amer J Cardiology* 77:867-870.