Religiosity/Spirituality and Health

A Critical Review of the Evidence for Biological Pathways

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The authors review evidence regarding the biological processes that may link religiosity/spirituality to health. A growing body of observational evidence supports the hypothesis that links religiosity/spirituality to physiological processes. Although much of the earliest evidence came from cross-sectional studies with questionable generalizability and potential confounding, more recent research, with more representative samples and multivariate analysis, provides stronger evidence linking Judeo-Christian religious practices to blood pressure and immune function. The strongest evidence comes from randomized interventional trials reporting the beneficial physiological impact of meditation (primarily transcendental meditation). Overall, available evidence is generally consistent with the hypothesis that religiosity/spirituality is linked to health-related physiological processes—including cardiovascular, neuroendocrine, and immune function—although more solid evidence is needed.

Our goal in this article is to assess evidence for possible biological mediators of observed links between various health outcomes and religiosity/spirituality. Although religiosity/spirituality has not been a major focus of research interest in recent decades, the 20th century, in fact, began with the publication in 1902 of William James's classic series of Edinburgh lectures, *The Varieties of Religious Experience*, and his first lecture carries the title "Religion and Neurology." James made it clear that he meant to address not only religion in its formal sense but more broadly the feelings, acts, and experiences of individuals "so far as they apprehend themselves to stand in relation to whatever they may consider the divine" (James, 1902, p.31). James also commented on a need directly pertinent to the task of the present article: namely, working out "some psychophysical theory connecting spiritual values in general with determinate sorts of physiological change" (James, 1902, p.16).

In some respects, James was following the example of earlier classic work by Durkheim (1897/1951), in which religious affiliation was used as a major variable in the analysis of suicide. Although the psychology and biology in Durkheim's analysis are rudimentary and thus reflective of their time, the thrust of Durkheim's analysis was deeply perceptive, recognizing that shared religious participation and religious representations were fundamental integrative forces in society with unique capacities to direct and control individual motivation.

What happened between these great early works and the present day is relevant, too. In great part, any central interest in the psychobiological study of religion disappeared, largely in the context of the development of a more narrowly scientific ethos stressing natural science methods, pragmatism, and behaviorism. Under the influence of a variety of factors, however (e.g. the rise of postmodernist thought, disaffection with the limitations of laboratory studies of human behavior), the temper of the times in research perspectives has shifted in the recent past (Rosenau, 1992), and there has been a resurgence of interest in investigation of the potential impact of religious and spiritual factors on health outcomes. An important marker of this shift can be seen in the mixed reception that was accorded to Norman Cousins's initial description of the anatomy of his illness (Cousins, 1979), which emphasized the spiritual factors in recovery, and his later, more empirically oriented analysis of "the biology of hope and the healing power of the human spirit" (Cousins, 1989). Further evidence of the resurgence of interest in possible links between religiosity/spirituality and health can be seen in the growing number of research articles on this topic. As has been outlined in several recent reviews, a growing body of research points to links between aspects of religiosity/spirituality such as church attendance or religious beliefs and better physical and mental health as well as lower

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mortality (Ellison & Levin, 1998; Levin & Chatters, 1998; Matthews et al., 1998; Mueller, Plevak, & Rummans, 2001; Worthington, Kurusu, McCullogh, & Sandage, 1996). These links between religiosity/spirituality and health outcomes are not the primary focus in this article, but they provide the stimulus for our task—namely, to review and evaluate the available evidence linking religiosity/spirituality to biologic processes that may serve as mechanisms for any health effects of religiosity/spirituality.

In the following sections, we review existing data on relationships between religious/spiritual engagement and physiological parameters that may represent pathways through which aspects of religiosity affect health. To the extent that such relationships can be documented, then it will be appropriate to pursue the subsequent question of whether these documented linkages serve as mediators that connect religiosity/spirituality to health outcomes such as mortality. We focus first on studies bearing on Judeo-Christian religious practices and beliefs. We then examine evidence relating to studies bearing on various kinds of spiritually guided meditation practices common to Eastern religions. Finally, we discuss several multicomponent mind–body intervention programs that include aspects of meditation and/or relaxation and cognitive/emotional therapy that have been presented as including spiritual components.

Physiological Correlates of Religiosity/Spirituality

Criteria for Evaluation and Ranking

A levels-of-evidence ranking system was used to evaluate the available literature. Following the criteria outlined by Miller and Thoresen (2003, this issue), we assigned each study a letter grade (A–C, shown in brackets following study citation in the text); the study design and sampling methods were considered primary factors, followed by the measurement and analysis approaches. Each of the authors independently rated the various studies reported here. Ratings were then compared, disagreements discussed, and a consensus rating arrived at for each study. A score of A was assigned to studies published in a peer-reviewed scientific journal with a study design and methodology judged to be sufficiently sound to provide strong evidence linking religiosity/spirituality to the physiological parameters examined. In practice, studies with the strongest study designs (i.e., prospective or randomized design) were assigned a score of A, whereas a score of A/B was assigned to those whose strengths (e.g., longitudinal design) were somewhat weakened by other design features, such as lack of sample generalizeability or problematic analytic methods. A score of B was assigned to studies with generally sound methodology but at least one important methodological limitation that clouded interpretation of the findings (e.g., cross-sectional data, use of a clearly nonrepresentative sample). A score of B/C was assigned to a B study with several important methodological weaknesses that were not so severe as to undermine the ability to draw some conclusions. A score of C indicates a study with major methodological flaws that undermine the ability to draw conclusions from the data.

On the basis of the available literature, a set of 11 propositions relating to hypothesized relationships between religiosity/spirituality and aspects of biology were evaluated. For each proposition, a summary level-of-evidence score was assigned that reflected the extent of support for the proposition based on the set of studies with data relevant to that proposition. Again, following the criteria outlined by Miller and Thoresen (2003), we defined four levels of evidence scores: 3 = persuasive support for the proposition (i.e., at least three Category A studies exist showing support for the proposition or at least five studies with a combination of A and/or B scores); 2 = reasonable evidence (i.e., two Category A studies or a combination of three to four Category A and/or B studies); 1 = some evidence (i.e., at least one Category A study or at least two Category B studies); and 0 = insufficient support (i.e., current evidence does not meet criteria for even a 1 classification). As shown in Table 1, scores ranged from 3 to 1. For each proposition, Table 1 lists the major studies that form the basis for the level of evidence score.

Judeo-Christian Religious Practices

A surprisingly small number of studies analyze the biological correlates of Judeo-Christian religious practices. Most of these studies examined relationships to blood pressure, although a few also examined relationships to lipid profiles or immune function. On the basis of these studies, we present evidence related to three propositions: (a) that religiosity/spirituality is associated with lower blood pressure and less hypertension, (b) that religiosity/spirituality is associated with better lipid profiles (i.e., lower LDL and higher HDL cholesterol), and (c) that religiosity/spirituality is associated with better immune function.

The studies of blood pressure present a generally consistent pattern relating greater religious involvement to lower blood pressure and/or lower prevalence of hypertension. Religious involvement in these various studies was measured in terms of greater church attendance (Graham et al., 1978 [B]; Hixson, Gruchow, & Morgan, 1998 [B]; Koenig et al., 1998 [A/B]; Larson et al., 1989 [B]; Livingston et al., 1991 [B]; Scotch, 1963 [B/C]) or reported religious commitment (Hixson et al., 1998 [B]; Larson et al., 1989 [B]; Steffen, Hinderliter, Blumenthal, & Sherwood, 2001 [A/B]; Walsh, 1998 [C]) or involved a comparison of nuns to lay women (Timio et al., 1997 [B]). Of these studies, however, only two actually include prospective evidence linking initial religious involvement to lower subsequent blood pressure (Koenig et al., 1998; Timio et al., 1997); the remainder of the studies present cross-sectional data showing relationships between religious involvement and lower blood pressure.

Timio et al. (1997) presented 30-year follow-up data on patterns of blood pressure change, comparing a sample of nuns from a secluded order in six convents in Umbria (Italy) with a group of lay Italian women living nearby who volunteered for the study. The two groups are reported to be similar at baseline with respect to ethnic background,

Table 1
Propositions Regarding Relationships Between Religiosity/Spirituality and Physiology

Proposition	Study	Study grade	Level of evidence scores
	I. Judeo-Christian religious practices		
1. Religiosity/spirituality is associated with lower blood pressure and less hypertension.	Koenig et al., 1998	A/B	2
	Steffen Hinderliter, Blumenthal, & Sherwood, 2001	A/B	
	Timio et al., 1997	B	
	Hixson, Gruchow, & Morgan, 1998	B	
2. Religiosity/spirituality is associated with better lipid profiles.	Friedlander, Kark, Kaufmann, & Stein, 1985	B	1
	Friedlander, Kark, & Stein, 1987	B	
3. Religiosity/spirituality is associated with better immune function.	Koenig et al., 1997	A/B	2
	Woods, Antoni, Ironson, & Kling, 1999	A/B	
	Ironson et al., 2002	B	
	Sephton, Sapolsky, Kraemer, & Spiegel, 2000	B	
	Sephton, Koopman, Schaal, Thoresen, & Spiegel, 2001	B	
	II. Zen, yoga, meditation/relaxation practices		
4. Meditation/relaxation is associated with lower blood pressure.	Schneider et al., 1995	A	2.5
	Patel et al., 1985	A	
	Schmidt, Wijga, Von Zur Muhlen, Brabant, & Wagner, 1997	B/C	
	Sudsuang, Chentanez, & Veluvan, 1991	B/C	
	Benson, Rosner, Marzetta, & Klemchuk, 1974	B/C	
5. Meditation/relaxation is associated with lower cholesterol.	Patel et al., 1985	A	2
	Schmidt et al., 1997	B/C	
6. Meditation is associated with lower stress hormone levels.	Jevning, Wilson, & Davidson, 1978	B/C	2
	Sudsuang et al., 1991	B/C	
	Infante et al., 1998	B/C	
	Walton, Pugh, Gelderloos, & Macrae, 1995	B/C	
7. Meditation is associated with less oxidative stress.	Schneider et al., 1998	B	1
8. Meditation is associated with less blood pressure reactivity under challenge.	Wenneberg et al., 1997	A	1
9. Meditation is associated with less stress hormone reactivity under challenge.	MacLean et al., 1997	A	1
10. Meditation/relaxation is associated with differential patterns of brain activity.	Lou et al., 1999	B/C	2
	Lazar et al., 2000	B/C	
	Newberg et al., 2001	B/C	
	Jevning, Anand, Biedebach, & Fernando, 1996	B/C	
	Benson, Malhotra, Goldman, Jacobs, & Hopkins, 1990	C	
11. Meditation/relaxation is associated with better health outcomes in clinical patient populations.	Kabat-Zinn et al., 1998	A	3
	Kabat-Zinn et al., 1992	B/C	
	Garfinkel et al., 1998	A	
	Mandle et al., 1990	A	
	Schneider et al., 1995	A	

Note. Study grades are as follows: A = a study published in a peer-reviewed journal, with study design and methodology sufficiently sound to provide strong evidence linking religiosity/spirituality to the physiological parameters examined; A/B = an A study weakened by other design features; B = a study with a generally sound methodology but at least one important methodological limitation; B/C = a B study with several important methodological weaknesses but not so severe as to undermine the ability to draw some conclusions; C = a study with major methodological flaws that undermine the ability to draw conclusions from the data. Levels of evidence scores are as follows: 3 = Persuasive evidence (i.e., at least 3 category A studies); 2 = Reasonable evidence (i.e., 2 category A studies OR combination of 3–4 category A and B studies); 1 = Some evidence (i.e., at least 1 category A OR at least 2 category B studies).

area of residence, family history of hypertension, smoking, alcohol consumption, height, and weight. They were also reported to show similar patterns of change in weight and body mass indices and similar ages at menopause. These group similarities on factors known to influence blood pressure provide a degree of support for the interpretation of subsequent blood pressure differences reflecting the differential life experiences of the nuns (i.e., their secluded, religious life) as compared with the secular women. However, as the authors indicated, there are numerous lifestyle differences between these two groups that remain uncontrolled in the analyses. As a result, it is not possible to draw a definitive conclusion as to whether the difference in religious involvement between the nuns and secular women is the primary factor that led to the observed differences in age-related increase in blood pressure.

Koenig et al. (1998) reported on data from a population-based, longitudinal cohort study of older adults living in and around Durham, North Carolina. They found strong cross-sectional relationships between religious involvement and lower blood pressure for the full cohort of older adults, but the longitudinal data provide mixed evidence of a relationship between religious involvement and lower blood pressure, showing a significant association only between 1989–1990 religious activities and 1993–1994 blood pressure (but not for 1989 to 1989–1990 data). Longitudinal associations were also found to be largely restricted to certain population subgroups, specifically Blacks and younger members of the cohort. The strength of this study is its population-based sampling and longitudinal design; the one caveat with respect to the reported findings is the large number of statistical tests that are reported (108 by our count) and the fact that the actual number of statistically significant findings is not much beyond what might be expected on the basis of a 5% Type I error rate. Thus, although the data are intriguing and do point to a relationship between religious activity and lower blood pressure, they are less than compelling, and further testing of a small number of specific hypotheses is needed.

Overall, although a number of studies show a relationship between religious involvement and lower blood pressure, the bulk of the evidence stems from cross-sectional data. Some studies suffer from sampling based on specialized source populations or more generally nonrepresentative samples (e.g., Hixson et al., 1998; Scotch, 1963; Steffen et al., 2001; Walsh, 1998), although two recent studies do use representative samples of Blacks (Livingston, Levine, & Moore, 1991) or White males (Larson et al., 1989) and find cross-sectional evidence for lower blood pressure among those reporting greater religious involvement (either greater reported church attendance or greater importance of religion in their lives). On the basis of this evidence, Proposition 1 (that religiosity/spirituality is associated with lower blood pressure and less hypertension) received an evidence score of 2 (see Table 1).

Friedlander and colleagues have studied possible links between religiosity and lipids, comparing Orthodox Jews with secular individuals. In one study of adult residents of Jerusalem, Orthodox Jews were found to have lower total cholesterol, triglyceride, and LDL cholesterol levels, although these differences were found to be largely attributable to differences in diet (Friedlander, Kark, Kaufmann, & Stein, 1985 [B]). A subsequent study found similar differences between orthodox and secular adolescents (aged 17–18 years) (Friedlander, Kark, & Stein, 1987 [B]). In this later study, diet was not controlled, leaving open the possibility that, like the earlier study, the reported findings largely reflect confounding between religiosity and diet. On the basis of these data, Proposition 2 (that religiosity/spirituality is associated with better lipid profiles) received an evidence score of 1 (see Table 1).

In a number of recent studies, researchers have examined relationships between religiosity/spirituality and immune function. In one study of HIV-positive gay men, Woods, Antoni, Ironson, and Kling (1999 [A/B]) reported that religious behavior (e.g., prayer, attendance at services) was associated with higher T helper/inducer cell (CD4+) counts and higher CD4+ percentages. Related analyses from this research group have also shown that greater reported spirituality is associated with lower cortisol and that this relationship partially accounts for the relationship between spirituality and longer term survival with HIV (Ironson et al., 2002 [B]). In another study, this one of women with metastatic breast cancer, it was also found that those who gave high ratings to the importance of spiritual expression in their life had greater numbers of white blood cells and total lymphocyte counts (with greater counts of both helper and cytotoxic T cells; Sephton, Koopman, Schaal, Thoresen, & Spiegel, 2001 [B]). Consistent with this evidence suggesting better immune function in those who gave spiritual expression a high rating of importance, additional analyses from this study also indicated that evening cortisol levels were lower in these women than in the other women in the study (Sephton, Sapolsky, Kraemer, & Spiegel, 2000 [B]). Koenig et al. (1997 [A/B]) have also reported evidence linking religious involvement to immune parameters in a general population sample. In this study, Koenig et al. examined both cross-sectional and longitudinal associations between church attendance and various parameters of immune function. The strengths of this study include the use of a population-based cohort (the Durham, North Carolina, Established Populations for the Epidemiologic Study of the Elderly cohort), the large sample size ($N = 1{,}718$), and both cross-sectional and longitudinal data on religious attendance, as well as data for a number of potential confounding factors. However, the findings are somewhat mixed and provide relatively weak support for the hypothesis that greater religious involvement is associated with better immune function. In the multivariate models, after adjusting for potential confounders, a significant association was found only for the cross-sectional association between greater church attendance and lower levels of Il-6, a marker of inflammation; earlier reported levels of church attendance (from 1986 and 1989) were not significant predictors of Il-6. The obtained association was found only when Il-6 was examined as a dichotomous measure (i.e., those reporting greater church attendance were less likely to have Il-6 > 5 pg/ml); no relationship was seen for the continuous measure of Il-6. Furthermore, with the exception of neutrophils (which were negatively associated with church attendance), other immune parameters (alpha-1, alpha-2, beta globulin, gamma globulin, lymphocytes, D-dimer, percentage of high D-dimer) were unrelated to church attendance. Thus, although intriguing, the findings for Il-6 provide only weak support for the hypothesized relationship between religious involvement and immune function because they are not part of a larger pattern of association between church attendance and immune function. On the basis of this evidence, Proposition 3 (that religiosity/spirituality is associated with better immune function) received a summary evidence score of 2 (see Table 1).

Meditation Studies

Although there is a relative paucity of research on Judeo-Christian religious practices and biological processes, there is a considerably larger body of research on biological correlates of other religious practices such as meditation (a central component of many Eastern religions). The studies represent a mixture of (a) those that examine Zen, yoga, and transcendental meditation (TM) in relation to various physiological parameters using largely observational, nonrandomized designs and (b) a smaller subset of studies (all from a single group of investigators at the Maharishi International University) using randomized, experimental designs. Also relevant are three studies of the biological effects of meditation as an experimental manipulation without an explicitly spiritual element incorporated into the meditation activity (i.e., meditation does not appear to have been presented to study participants within a religiosity/spirituality framework; Jacobs, Benson, & Friedman, 1996; Kiecolt-Glaser et al., 1985; Patel et al., 1985). For several other studies where TM was the intervention, it is unclear how much of the broader religiosity/spirituality framework of TM was actually a component of the intervention (Benson, Rosner, Marzetta, & Klemchuk, 1974; Schneider et al., 1995).

We derived and evaluated eight different propositions, covering postulated relationships to cardiovascular function (blood pressure and cholesterol), measures of oxidative stress and stress hormones, and patterns of brain activity (see Table 1, Propositions 4–11). The strongest evidence relates to the postulated relationship between meditation and lower cardiovascular risks (i.e., lower blood pressure and cholesterol). Only Schneider et al. (1995 [A]) and Patel et al. (1985 [A]) used fully randomized designs. However, the Patel et al. study falls into the category of studies without explicit religiosity/spirituality frameworks for their meditation interventions and thus provides evidence for effects of meditation but without the attendant religiosity/spirituality element in other studies discussed below. The Schneider et al. study is also somewhat ambiguous with respect to the extent of the religiosity/spirituality implication in the meditation intervention. They reported on a randomized trial designed to test the effectiveness of TM to reduce blood pressure in mildly hypertensive older African American adults (aged 55 years and over) recruited from primary care centers. Subjects were randomized to three months of TM versus muscle relaxation versus lifestyle education classes. At the end of the three-month follow-up, subjects randomized to TM had significantly reduced systolic and diastolic blood pressure; TM was found to be approximately twice as effective as relaxation, and both TM and relaxation were more effective than the education classes. This study is noteworthy in terms of its target population—older African-Americans—which stands in stark contrast to the largely White, male, college-student populations analyzed in a majority of the other studies. It is also noteworthy for its rigorous methodology, including a randomized design, intention-to-treat analyses, and extensive consideration of potential confounders. However, it is not clear exactly how much of the more spiritual framework of TM was incorporated into the intervention.

The Patel et al. (1985) study, as noted above, was a randomized, longitudinal study of the impact of an eight-week meditation/relaxation intervention that does not appear to have explicitly included broader religiosity/spirituality elements. Patel et al. examined the effects of their meditation/relaxation intervention in a sample of subjects identified as being at high risk for cardiovascular disease by virtue of their having two or three of the three major risk factors for cardiovascular disease (i.e., smoking, blood pressure $>$ 140/90 mmHG, or cholesterol $>$ 244mg/100ml). Subjects (N = 230) were randomized to eight sessions (one per week) of treatment (health education and meditation/relaxation training) or control (health education only). Subjects in the meditation/relaxation group exhibited significantly greater decreases in blood pressure at eight weeks, eight months, and four years postintervention and lower cholesterol levels at eight weeks and eight months postintervetion. Patel et al. also reported electrocardiograph evidence for greater ischemia in the control group at four years postintervention as well as greater incidence of cardiac events.

Three additional relevant studies are observational, comparing groups of self-selected practitioners of various forms of meditation (e.g., Zen, TM, Buddhist) to self-selected groups of nonpractitioners. In each of these studies, the meditation activity more explicitly embodied a religiosity/spirituality framework. As with other such observational, nonrandomized studies discussed below (e.g., comparing novice TM practitioners to expert TM practitioners), these designs suffer from the Achilles heel of potential selection bias: That is, self-selected meditation versus nonmeditation groups may differ on characteristics other than meditation, and these other factors may well serve as confounders of the observed association between meditation and physiology. Thus, although these studies also suggest relationships between meditation and lower blood pressure (Benson et al., 1974 [B/C]; Schmidt, Wijga, Von Zur Muhlen, Brabant, & Wagner, 1997 [B/C]; Sudsuang, Chentanez, & Veluvan, 1991 [B/C]) and lower cholesterol (Schmidt et al., 1997 [B/C]), their methodological weaknesses reduce the weight of their evidence, as indicated by their scores of B rather than A. On the basis of the cumulated evidence, Propositions 4 and 5 (that meditation/relaxation is associated with lower blood pressure and that meditation/relaxation is associated with lower cholesterol) received summary evidence scores of 2.5 and 2, respectively, indicating there is at least reasonable evidence for these propositions (see Table 1).

Another set of studies provides evidence on links between meditation and levels of stress hormones and/or markers of oxidative stress (see Table 1, Propositions 6 and 7). All of these studies embody observational designs, although four do include longitudinal data. Jevning, Wilson, and Davidson (1978 [B/C]); Sudsuang et al. (1991 [B/C]); Schmidt et al. (1997 [B/C]); and Werner et al. (1986 [B]) each report data on longitudinal changes in physiological profiles for self-selected meditation and nonmeditation groups.

Schmidt et al. (1997) compared patterns of change for a range of physiological parameters in a group of individuals participating in a three-month intensive yoga training program in Sweden, comparing them with a control group of age- and gender-matched residents of Hanover, Germany. Yoga participants exhibited greater reductions in blood pressure, cholesterol, fibrinogen, and body mass but showed increases in cortisol excretion. Possible group differences on factors other than yoga participation (e.g., dietary changes) were not factored into the analyses, making it difficult to draw strong conclusions from these data.

Sudsuang et al. (1991) compared change for a group of Thai college students who elected to undertake a two-month program of meditation training and a group of students who did not. At the end of the two-month period, the meditation group exhibited greater decreases in cortisol, pulse rate, and systolic and diastolic blood pressure. Jevning et al. (1978) also examined changes in cortisol activity in a group of novice TM practitioners, the initial cortisol assessments being taken before the group began TM and compared with measurements taken after two to five months of TM practice. In this study, the novice group was also compared with a group of long-term TM practitioners. The results are interesting in that the long-term TM group exhibited the lowest cortisol, with the novice group showing values at their second (post-TM initiation) assessment falling midway between their initial (pre-TM) assessment and those of the long-term practitioners. The pattern of these findings raises the question of whether duration of practice may influence the extent of physiological effects, a point that should be borne in mind with respect to a number of randomized trials of TM (discussed below) that reflect results of relatively short-term TM initiation in all cases (three to four months). The final longitudinal study, by Werner et al. (1986), reported three-year longitudinal data for 11 male practitioners of TM showing reductions in plasma thyroid-stimulating hormone (TSH), growth hormone (GH), and prolactin but no change in cortisol, T4, or T3 levels.

The remainder of the pertinent studies are cross-sectional and compare self-selected TM (or other meditation program) practitioners to nonpractitioners (Infante et al., 1998 [B/C]; Schneider et al., 1998 [B]; Walton, Pugh, Gelderloos, & Macrae, 1995 [B/C]). Infante et al. (1998) found that TM practitioners had lower morning levels of adrenocorticotropic hormone, although their patterns of cortisol activity did not differ from non-TM practitioners. A similar cross-sectional comparison of TM practitioners with nonpractitioners by Walton et al. (1995) found that the non-TM group had significantly greater urinary excretion of cortisol (especially for waking hours), along with a lower dehydroepiandrosterone sulfate (DHEA-S)/cortisol ratio (DHEA-S having been postulated to function as an hypothalamic-pituitary-adrenocortical axis antagonist). The non-TM group was also found to excrete more aldosterone, more 5-hydroxyindoleacetic acid (5-HIAA, a serotonin metabolite), more vanillylmandelic acid (VMA, a norepinephrine metabolite), and more of various electrolytes (Na^+, Ca^{2+}, Zn^{2+}, and Na^+/K^+ ratio). Recently, Schneider et al. (1998) reported on cross-sectional data for 18 long-term TM practitioners and 23 nonpractitioners, comparing levels of lipid peroxide as a marker for potential group differences in oxidative stress (i.e., free radical activity). The TM practitioners were found to have 15% lower levels of serum lipid peroxides ($p = .026$). Although these studies suffer from the problem of potential confounding of observed TM/non-TM group differences with group differences on other characteristics, the pattern of findings is generally consistent with the hypothesis that TM leads to a profile of generally lower physiological activation, a profile that is generally thought to be associated with lower health risks. As a result, Proposition 6 (that meditation is associated with lower stress hormones) received an evidence score of 2, whereas Proposition 7 (that meditation is associated with less oxidative stress) received a score of 1 (see Table 1).

In addition to these observational data, there is a small but intriguing literature on possible TM effects on response to challenge (see Table 1, Propositions 8 and 9). One report focuses on cardiovascular reactivity (Wenneberg et al., 1997 [A]); the other focuses on stress hormone reactivity (MacLean et al., 1997 [A]). It appears that these two articles may, in fact, represent the same samples and certainly reflect identical protocols. Each of these articles reports on a study of the impact of a four-month program of TM versus stress education classes (SEC) for groups of men randomly assigned to these treatment groups. In each case, the groups were assessed for differences in physiological response to a standardized laboratory challenge protocol that included mental arithmetic, a star-tracing task, and isometric handgrip.

Wenneberg et al. (1997 [A]) reported on cardiovascular effects, no significant group differences being seen for blood pressure either during ambulatory monitoring or during a standardized laboratory challenge session. A high compliance TM subgroup did have lower ambulatory diastolic blood pressure, and comparison of this group to the noncompliant subgroup revealed no significant differences on other physiological variables or potential confounders. However, such subgroup analyses must be interpreted with caution, as they no longer reflect the strength of the original randomization given that the subjects self-selected into the compliant group (or not). On the basis of this study, Proposition 8 (that meditation is associated with less blood pressure reactivity under challenge) received an evidence score of 1.

MacLean et al. (1994 [A], 1997 [A]) reported on endocrine differences observed between the TM and SEC groups, including plasma cortisol, TSH, GH, and testosterone. The findings are relatively complex, and interested readers are encouraged to examine the more detailed article (MacLean et al., 1997). Among other things, it is important to bear in mind the relatively small sample sizes in the two groups ($n = 13$ for the SEC group; $n = 16$ for the TM group), as these relatively small samples reduce the statistical power of the study to detect group differences. Indeed, in a number of cases, a number of apparent trends did not reach statistical significance but may be worthy of further investigation. A further point of note is the fact that, as the authors indicate, the pre- and postintervention assessments are unfortunately also confounded with differences in the academic calendar: The preintervention period is midyear, whereas the postintervention period is just before final exams.

The group receiving TM exhibited a lower prechallenge baseline cortisol at the time of their postintervention challenge session, a result that was also paired with evidence of greater cortisol reactivity (i.e., greater total area under the curve in response to the challenge protocol). Unfortunately, as the authors acknowledged, attrition from the original randomized groups resulted in preintervention differences in cortisol between the TM and SEC groups, with the TM group showing a significantly higher baseline cortisol level (13.9ug/dl in the TM group vs. 9.5ug/dl in the SEC group, $p = .03$). From the data presented, it appears that the reduction in baseline cortisol in the TM group may reflect regression to the mean as much as the intervention itself, because their postintervention cortisol levels are similar to those seen in the SEC group pre- and postintervention. It is also worth noting that the lower baseline cortisol at postintervention for the TM group, whatever its source (e.g., true intervention effect or regression to mean), may account for the related finding of greater apparent reactivity postintervention in the TM group, given that it is not uncommon to find that higher baseline values are frequently associated with less overall response. Thus, with their now lower baseline cortisol, the TM group exhibited greater total area under the curve in response to the challenge, a pattern that has been suggested to be more adaptive (Sapolsky, 1990). The authors also noted that plasma serotonin values in the TM group showed declines for both baseline and response to stress values.

Other findings reported by MacLean et al. (1997 [A]) include apparent SEC versus TM differences in patterns of change in TSH and GH reactivity to the challenge protocol from pre- to postintervention. For TSH, both groups exhibit smaller overall response to challenge postintervention; however, the TM group's response profile was negative (i.e., values dropped below baseline over the course of the challenge), whereas the SEC group continued to show a positive response (i.e., increased in TSH over baseline). For GH, the SEC group appeared to show a decreased level of reactivity, whereas the TM group showed an apparent increased reactivity. However, these latter findings may also be influenced by what appear to be group differences in baseline levels of GH, with the SEC group showing a higher baseline whereas the TM group's baseline decreased (perhaps again contributing to the greater apparent response to the challenge). No major effects were reported for testosterone. On the basis of this study, Proposition 9 (that meditation is associated with less stress hormone reactivity under challenge) received an evidence score of 1.

One final area of growing research interest relates to the assessment of the effects of meditation/relaxation activities on brain activities (see Table 1, Proposition 10). In several recent studies, researchers have examined differences in brain activity using various functional imaging techniques, such as positron emission tomography (PET), single photon emission computed tomography (SPECT), and functional magnetic resonance imaging (fMRI). In each case, small samples of individuals experienced in a particular type of meditation were evaluated to determine which patterns of brain activity were associated with such meditation. Lou et al. (1999 [B/C]) used PET scanning technology to examine differences in regional brain activation in nine yoga practitioners under various conditions (e.g., meditation, resting state, auditory stimulation). Regional brain activation was reported to differ across these conditions, with meditation-associated activation in posterior and associative cortices known to participate in imagery tasks. Lazar et al (2000, [B/C]) also reported that fMRI data for five subjects with at least four years of experience in Kundalini meditation indicated that practicing such meditation activates neural structures involved in attention (i.e., frontal and parietal cortex) and control of the autonomic nervous system (i.e., pregenual anterior cingulate, amygdala, midbrain, and hypothalamus). Similar findings have also been reported by Newberg et al. (2001 [B/C]) based on SPECT data for eight Tibetan Buddhist meditators. The data showed evidence for increased regional cerebral blood flow in the cingulate gyrus, inferior and orbital frontal cortex, dorsolateral prefrontal cortex, and thalamus.

These data from functional imaging studies are also consistent with evidence from studies using older technology that suggested that meditation may result in lower levels of physiological activation (e.g., lower blood pressure and pulse, lower endocrine activity, lower body metabolism) through differential effects on patterns of brain activity. Jevning, Anand, Biedebach, and Fernando (1996 [B/C]) reported increased patterns of frontal and occipital cerebral blood flow associated with TM, a finding they interpreted as being consistent with "a patterned response sub-serving needs of increased cerebral activity" (p.399). In another study, Jacobs et al. (1996 [C]) examined the effects of relaxation (without an explicit religiosity/spirituality component) by comparing electroencephalogram (EEG) recordings for a small group of volunteers ($n = 20$) in response to a relaxation tape versus a control tape condition. They reported finding reductions in frontal EEG beta activity in response to the relaxation tape, whereas no differences were seen for temporal, central, or parietal areas. The authors suggested that this specific pattern of differences may relate to relaxation response effects on cortical brain regions with connections to limbic/hypothalamic structures that play an important role in emotion regulation and that are involved in fight-or-flight responses. And data from three case reports for Tibetan Buddhist monks also provide evidence that several different meditative practices were associated with changes in body metabolism as well as EEG evidence of increased beta activity (Benson, Malhotra, Goldman, Jacobs, & Hopkins, 1990 [C]).

These studies represent more recent examples of a larger and older body of research on EEG effects of meditation and/or biofeedback, a literature that dates back to the 1970s, when studies of meditative spiritual practices and biofeedback were popular (American Psychiatric Association Task Force on Biofeedback, 1980; Barber et al., 1971; Hirai, 1974; Marcer, 1986). Typical reproducible physiological responses associated with meditation/biofeedback from those earlier studies include (a) increased alpha (relaxation) and theta (hippocampal) wave EEG patterns, (b) decreased respiratory rate and oxygen consumption, and (c) reduced blood pressure (systolic and/or diastolic). On the basis of evidence from both the newer imaging studies as well as the older EEG studies, Proposition 10 (that meditation/relaxation is associated with differential patterns of brain activity) received an evidence score of 2 (see Table 1).

Interventions in Clinical Populations

A growing body of research focuses on the effects of meditation/relaxation interventions in clinical populations. The body of evidence in this area reflects a series of studies that vary in terms of both the specific clinical populations that are examined and the specific outcomes that are evaluated. Because no single outcome was examined in more than one study, a general single overall proposition was evaluated: that these interventions appear to demonstrate effects on physiological and/or functional health outcomes in patient populations (see Table 1, Proposition 11).

Two general categories of research show relationships between mind–body practices and patterns of biological activity in clinical populations. In one set of studies, Kabat-Zinn and colleagues (Kabat-Zinn et al., 1992 [B/C], 1998 [A]) used a meditation-based stress reduction program, referred to as *mindfulness meditation*, whereas other researchers, in a second category of studies, examined biological impacts of various types of relaxation and/or meditation/yoga training in a series of different clinical populations. The religiosity/spirituality component of these interventions is not always a direct, explicit focus of the research; rather, it is indirectly inferred from the discussion of the intervention and its impact on participants. We elected to include them in this review as a stimulus to further consideration in future research of potential religiosity/spirituality components of such interventions in patient populations.

The studies by Kabat-Zinn and colleagues (1992 [B/C], 1998 [A]) reported on a meditation-based stress reduction program, or mindfulness meditation. Mindfulness meditation is designed to help practitioners cultivate greater concentration and relaxation and has been reported to result in increased reports of spiritual experiences (Astin, 1997). It differs from TM in that practitioners are trained to attend to a wide range of changing objects of attention rather than restricting one's focus to a single object, such as a mantra. In various studies, Kabat-Zinn and colleagues have reported that mindfulness meditation programs have resulted in reductions in anxiety and depression in patients with generalized anxiety or panic disorder (Kabat-Zinn et al., 1992 [B/C]) and faster clearing of psoriasis (in conjunction with phototherapy; Kabat-Zinn et al., 1998 [A]).

The second, more general type of mind–body investigation is represented by studies of the biological impacts of relaxation and meditation/yoga training. Garfinkel et al. (1998 [A]), in a randomized single-blind study of 42 carpal-tunnel patients, reported that a yoga-based eight-week intervention resulted in significant improvements in grip strength and reductions in pain. Mandle et al. (1990 [A]) examined differences in self- and staff-assessed anxiety and pain in patients undergoing femoral artery angiographies when patients were randomly assigned to one of three conditions during the angiography: listening to a relaxation audiotape, listening to a music audiotape, listening to a blank audiotape. Patients in the relaxation audiotape condition reported less anxiety and pain than those with music or blank audiotapes and were similarly assessed by staff who were blinded to the patients' audiotape assignment. However, no differences in physiological parameters such as blood pressure or heart rate were seen. A number of studies have also tested the effectiveness of various meditation/yoga interventions in reducing blood pressure among people who have received a diagnosis of hypertension. Older studies most frequently used a pre/post design, where changes in blood pressure were assessed by taking measurements before and after patients were trained to perform various meditation/yoga practices. Findings from these earlier studies were somewhat mixed, with some reporting reductions in blood pressure (Patel & North, 1975 [B/C]; Sundar et al, 1984 [B/C]) and others not (Hafner, 1982 [B/C]; Pollack, Case, Weber, & Laragh, 1977 [B/C]). As noted in the earlier discussion of evidence from the research group at the Maharishi International University, one randomized clinical trial of TM in older people with hypertension demonstrated that TM was twice as effective as relaxation or education only in reducing blood pressure (Schneider et al, 1995 [A]). On the basis of these studies, Proposition 11 (that meditation/relaxation is associated with better health outcomes in clinical patient populations) received an evidence score of 3. However, it is important to bear in mind that this summary assessment of Proposition 11 actually reflects evidence relating to a number of different health outcomes rather than a body of evidence for any specific outcome. Indeed, although there is a body of evidence supporting the general proposition, in fact, there is generally no more than one A-level study providing support for a link between a given intervention and a specific health outcome. Thus, any final assessment of the potential benefits of a meditation/relaxation intervention with respect to a given health outcome will require further research evidence.

Summary and Conclusions

The literature we have reviewed has several striking features. First, relatively limited attention has been given to the physiological aspects of religious/spiritual orientation. Second, for the most part, the studies that do engage this question have been conducted on special populations and/or Eastern forms of spiritual practice. Available data for Judeo-Christian religious practices are largely based on evaluation of relationships between reported frequency of church attendance and blood pressure or immune function. Clearly, there is a need for greater attention to other specific aspects of Judeo-Christian religious practices, including individual and group prayer, reading of religious texts, and various aspects of religious services. The evidence discussed herein provides what might best be seen as an initial, relatively sparse, and somewhat mixed body of evidence suggesting that aspects of religiosity may indeed be linked to physiological processes related to health.

However, evidence of such linkages is especially sparse and weak with respect to aspects of Judeo-Christian religions, relying to date on largely cross-sectional studies of questionable generalizability due to the selective nature of the samples. There is somewhat better (although still mixed) evidence that meditation may be associated with lower physiological activation. Again, however, the available data come largely from nonrandomized observational studies with serious issues of confounding and generalizability that undercut the impact of the reported findings. The strongest data come from the small number of randomized trials reporting generally beneficial physiological impacts of interventions involving meditation (primarily studies involving transcendental meditation) or multicomponent interventions including meditation, relaxation, and/or other cognitive/emotional supportive group therapy.

As we attempt to evaluate this literature and to draw even preliminary conclusions, it is important to bear in mind that the available evidence reflects only those studies that were actually published. To the extent that negative and/or nonsignificant findings are less likely to appear in published format, it is possible that there is a larger body of data indicating a lack of association between religiosity and physiological processes than is evident from the available literature.

With that caveat in mind, a prudent interpretation of the data might be that the evidence reported to date is generally consistent with the hypothesis that aspects of religiosity/spirituality may indeed be linked to physiological processes—including cardiovascular, neuroendocrine, and immune function—that are importantly related to health. However, considerably more research is needed. Some of the important issues that will need to be addressed in future research are described below.

Sample Representativeness and Issues of Confounding That Have Plagued Previous Research

Although completely randomized studies provide perhaps the strongest methodological controls for concerns regarding self-selection into groups and possible confounding with other factors, such designs cannot be seen as the only viable approach, as they are likely to be impossible in many cases (e.g., where beliefs and attitudes are of interest as compared with behaviors like meditation). However, lack of randomization does not preclude stronger methodological approaches to investigating hypothesized relationships between aspects of religiosity and physiology. Foremost, greater attention to issues of confounding (including measurement and analysis of potential confounders) as well as less reliance on volunteer or special groups will lead to stronger observational studies. Indeed, observational studies can be a source of important evidence on hypothesized relationships between religiosity/spirituality and physiology if such designs include more rigorous attention to issues of sampling and controls for potential confounding factors.

Careful Disaggregation of the Concept of Religiosity/Spirituality Itself, Including a Clearer Specification of the Dimensions of Religiosity That Might Be Differentially Related to Physiological Processes and to Health Outcomes

Some of these dimensions are distinguished in the literature: for example, belief in a higher power as distinct from church/worship attendance or identification or affiliation with a particular denomination or faith. But these dimensions need to be more systematically analyzed, allowing for such aspects as the exclusivity and extremity of belief or commitment. There is no reason to think that only positive physiological and health consequences flow from religious engagement, and the identification of the multiple dimensions of such experience would allow for attention to both negative and positive physiological/health outcomes (e.g., potentially negative outcomes associated with religiosity/spirituality commitment include feeling punished by God or anger at God, conflicts with other congregation members, religious doubts, and religious passivity).

Specification of Possible Population Variation in Patterns of Relationships (e.g., Individual/Subgroup Differences by Age, Gender, Social Class, or Ethnic or Minority Status)

Does faith matter more or differently in different sectors? Given the concentration of effort thus far on specialized groups, it becomes important to be able to answer the question Do different kinds of religious experience characterize differently placed social groups, and does this religious experience have different consequences (in particular, physiological consequences) in these groups (e.g., for the young and the aged, for lower socioeconomic-status respondents, among those with existing health problems)?

Examination of Physiological Profiles

For the most part, prior studies have focused on singular physiological measures (e.g., blood pressure or pulse rate). However, as even the modest literature reported here on the biological impacts of religiosity/spirituality demonstrates, those impacts do not appear to be restricted to only blood pressure or even to the cardiovascular system. Rather, evidence (albeit modest) points to effects on various biological regulatory systems, including the immune system, metabolic parameters, and the central nervous system. Thus future research should include broader assessments of biological impacts of religiosity/spirituality, including assessments across multiple regulatory systems rather than assessments that focus on one or another of these interrelated systems. Studies that incorporate such a multisystems view of biological health will be essential if a clearer understanding of potential biological mediators of R/S effects on health is to be gained.

Finally, it is worth noting that the present time may be particularly opportune for an expanded program of research on biological mechanisms. Recent innovations in measurement of physiological parameters, including the development of less invasive protocols (e.g., salivary cortisol protocols) as well as protocols to permit assessments of brain function (e.g., functional brain imaging), offer a growing number of exciting new avenues for research on physiological mechanisms. Analysis of neuroanatomical sites of activity activated in processing religiosity/spirituality information is just beginning (e.g., see Lou et al., 1999). Such research offers the potential for identifying components of sensory and/or cognitive inputs associated with religiosity/spirituality experiences, thoughts, beliefs, or practices as well as the cognitive and emotional processing circuits. Such information could then be linked to systematic investigation of neuroendocrine and immunological response pathways. Continuing technological innovation also offers the potential for developing assessment protocols that are less invasive and/or less time consuming and will aid in successfully implementing studies using less selected, volunteer samples.

In summary, current evidence suggests that aspects of religiosity/spirituality may indeed be linked to important physiological regulatory processes. However, additional research is needed that encompasses stronger research methodology, including not only the use of experimental designs where feasible but also, importantly, for the observational designs, a greater attempt to include more representative samples (a common weakness of much of the previous research resting heavily on this latter feature of the evidence). In addition, a more thorough examination of aspects of spirituality other than meditation would seem indicated. Such research has the potential to provide important insights into possible relationships between aspects of religiosity/spirituality and physiological processes that affect health and well-being.

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