

between Swedish and American cultures, it would be interesting to further test this hypothesis by comparing the results in Sweden and the United States with a population drawn more from the openly mystical contexts found in some African or aboriginal cultures.

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Dr. Borg and Colleagues Reply

TO THE EDITOR: We appreciate that Dr. Hall and colleagues draw attention to the problem of defining the concepts of “spirituality” and “religion.” Several multidimensional or pluralistic definition systems of religion have indeed been proposed over the years. However, none of them offers a perfect solution to the need of operational tools in research on a possible biological underpinning of religious and spiritual behavior.

The authors criticize our article for using the terms “religion” and “spirituality” interchangeably. However, we did not use the concept “religion” in the article. Rather, the concept “religious behavior,” which is operationally defined in the literature (1), denotes cognitive and emotional behavior associated with (the individual’s relationship to their) religious beliefs. The term “spirituality” has been used in a wider context, including internal, subjective experiences, and has not been consistently defined by operational criteria. It is worth noting that the concept of spirituality is not necessarily linked to organized religion.

“Religious behavior” and “spirituality” are both covered by the personality subscale of the Spiritual Acceptance Scale, which was used in our study. The Spiritual Acceptance Scale consists of 13 items that include cognitive affirmation and values as well as subjective experiences of mystical quality. Thus, the definition of religion at a sociocultural level, as suggested by Dr. Hall and colleagues, is not covered by the scale used in our study and belongs to a different discussion.

Another part of Dr. Hall and colleagues’ criticism is their interpretation that aspects of mystical experiences can be mediated by the central serotonin system. We do not suggest that the serotonin system per se mediates mystical experiences but instead may act as a sensory filter (2). Low serotonin 5-HT_{1A} receptor binding potential may be associated with a low filter function, thus paving the way for sensory stimuli

otherwise not experienced. The more narrow focus on mystical experiences in this part of the discussion in our article (pp. 1967–1968) was given by comparisons made with pharmacological mechanisms causing similar experiences in man.

Finally, we agree with Dr. Hall and colleagues that it would be interesting to repeat this study in different populations. Epidemiological studies provide support for the view that religious behavior (in a more narrow sense) and spirituality (in a wider sense) are influenced by both genetic and environmental factors (3, 4). Given the previously demonstrated genetic contribution to religious behavior and spirituality, it is a promising strategy to use interindividual variability in neuroreceptor binding as a tool to approach the multifaceted question of why people vary in spiritual zeal and also within the same religious belief system.

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Conflict-of-Interest Charge

TO THE EDITOR: In the review by Robert T. Rubin, M.D., Ph.D (1), of *Psychoneuroendocrinology: The Scientific Basis of Clinical Practice* (2), he charged that I, a coeditor of the book, have an undisclosed conflict of interest: “Also troublesome is Rothschild’s undisclosed financial interest in Corcept Therapeutics, which is attempting to establish mifepristone as an antidepressant.” There are only three sentences in this 588-page book regarding studies of mifepristone for the treatment of psychotic depression:

Another interesting strategy is the progesterone receptor antagonist mifepristone (RU 486), which at high concentrations is an effective antagonist of glucocorticoid action in vivo and in vitro (Lamberts et al. 1984; Proux-Ferland et al. 1982). Mifepristone has been observed to be useful in rapidly reversing psychotic depression secondary to Cushing’s syndrome (Nieman et al. 1985; Van Der Lely et al. 1991) and in patients with psychotic major depression (Belanoff et al. 2001; Rothschild and Belanoff 2000). Studies of mifepristone for the treatment of psychotic major depression using a double-blind, placebo-controlled paradigm are currently in progress at our center and several others across the country.

To set the record straight, I do not now and never have owned stock in Corcept Therapeutics. I served briefly as a

consultant to Corcept Therapeutics (October 2000 to March 2001) regarding the methodology of a clinical trial of mifepristone for the treatment of psychotic depression. In addition, I was an investigator at the University of Massachusetts Medical School for multisite clinical trials of mifepristone for the treatment of psychotic depression, a fact that is obvious from the relevant paragraph in the book.

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Dr. Rubin Replies

TO THE EDITOR: I appreciate the opportunity to reply to several issues raised by Dr. Rothschild. First is my taking him to task for nondisclosure of a financial conflict of interest. When I wrote my review of Dr. Rothschild's chapter, he had declared "a financial interest in Corcept Therapeutics" in a published article (1). Only recently did he clarify that "in the past, he has been a consultant to and received research grants from Corcept Therapeutics" (2). If Dr. Rothschild had provided a similar statement in the chapter in question, this issue would not have arisen.

Second is whether financial disclosures should be required in book chapters. I believe they should. Financial disclosure is a major issue now; e.g., following a recent exposé of the nondisclosure of several major financial conflicts in a review of depression treatments (3), the Nature Publishing Group extended its disclosure requirement to review articles (4). Other journals have expanded their disclosure policies to cover all published material, and public interest groups have lent their voice in support (5). Nevertheless, violations continue to surface; e.g., the controversy over nondisclosure in an article in the *Lancet* suggesting a link between measles-mumps-rubella vaccinations and pervasive developmental disorder in children (6). Even full disclosure, however, is not a panacea (7).

Third is the questionable efficacy of mifepristone in psychotic depression in contrast to Dr. Rothschild's statement of its use in "rapidly reversing psychotic major depression." In the two published studies on this issue, there was no significant drug effect (1, 8). In the first study (8), two placebo cells were eliminated because they were considered a drug carry-over effect, and an independent-samples analysis apparently was performed, even though the data were paired (subjects were their own control subjects). My independent, paired-data analysis yielded a clearly nonsignificant difference. In the second study, no statistical analysis at all was presented. My analysis of those outcome data again yielded a clearly nonsignificant difference. As well, the April 2004 initial public offering filed with the Securities and Exchange Commission by Corcept Therapeutics (9) indicates that even in large double-blind trials, only a small number of patients became asymptomatic, with no significant difference between drug and placebo. Does this medication, then, warrant the paean of "ECT in a bottle" (10)?

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Potential for Misuse of Sedatives

TO THE EDITOR: The literature review by Ripu D. Jindal, M.D., et al. (1) highlighted important and timely issues concerning the public health problem of insomnia and the lack of literature on the maintenance treatment of insomnia. Although the authors discussed the ongoing debate on the long-term use of benzodiazepines, they cited a range of clinical and biological studies suggesting that "the liability of abuse of benzodiazepines is generally low." We would also stress the need to consider data on sedative abuse from large-scale community surveys that were not included in the review. The lifetime prevalence of sedative abuse/dependence was 1.2% in the Epidemiologic Catchment Area study (2). Recently, data from the National Comorbidity Survey suggested a lifetime prevalence of sedative dependence at 0.5%, as well as 7.1% of the U.S. population reporting the nonprescription use of sedatives (3). Respondents with sedative misuse and dependence had high levels of psychopathology and an increased risk of suicidal ideation/attempts (3).

To further examine this issue, we conducted analysis of a large community sample (N=8,116, ages 15–64) in Ontario, Canada, that had the same methodology as the National Comorbidity Survey (4). In the Ontario sample, 4.3% of the respondents reported nonprescription use of sedative/hypnotic medications, and 0.3% of the sample met DSM-III-R criteria for sedative abuse or dependence. Lifetime sedative misuse had a significant association with past-year suicidal ideation (odds ratio=2.34, 95% confidence interval [CI]=1.15–4.73), lifetime DSM-III-R major depression (odds ratio=4.47, 95% CI=3.00–6.66), and any lifetime anxiety disorder diagnosis (social phobia, simple phobia, generalized anxiety disorder, panic disorder, agoraphobia) (odds ratio=3.00, 95% CI=