



A Response to the Paal et al. Rejoinder: Religiosity and Risk of Parkinson’s Disease in England and the USA

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Accepted: 27 December 2022 / Published online: 6 January 2023

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Abstract

This commentary provides a response to the rejoinder by Paal et al. (Journal of Religion and Health. <https://doi.org/10.1007/s10943-022-01726-y>, 2023), regarding the research of Otaiku (Journal of Religion and Health. <https://doi.org/10.1007/s10943-022-01603-8>, 2022) “Religiosity and risk of Parkinson’s disease in England and the USA.” After providing a brief overview of Otaiku’s work, the commentary then addresses each of Paal et al.’s arguments. While agreeing that more research needs to be undertaken, this commentary concludes that Otaiku’s research findings are well founded, suggesting that greater religiosity may lower the risk of PD.

Keywords Parkinson’s disease · Religiosity · Abidemi I. Otaiku

Introduction

In this commentary, I first review the study and results reported by Abidemi Otaiku (2022) in some detail; briefly review the rejoinder to Otaiku submitted by Paal and colleagues (2023) in their critique of the study; and then comment on that critique. Reviewing in detail the study design, analysis, and findings is necessary in order to provide a background on which to understand the concerns noted in the rejoinder and my comments in response to those concerns.

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The Study

In an article published online in the *Journal of Religion and Health* on June 28, 2022, Abidemi Otaiku from the department of neurology at Birmingham City Hospital and Center for Human Brain Health at the University of Birmingham, Birmingham, UK, reported an analysis of prospective data on 9796 participants with the purpose of examining the effect of religiosity on the future risk of developing Parkinson's disease (PD) in the UK and the USA. Data were obtained from two well-known and reputable longitudinal studies, the English Longitudinal Study of Aging (ELSA, $n=7124$) and the Midlife in the US Study (MIDUS, $n=2672$). The average age of participants at baseline was 65 years in the ELSA cohort and 55 years in the MIDUS cohort; 56% were women and 81% Christian in the combined samples. All participants were free from PD at baseline and followed for an average of 8.1 years. Baseline was July 2010 for the ELSA (with follow-up through July 2019) and 2004–2006 for the MIDUS (with follow-up through June 2014). The development of PD across the waves of data collection was determined by self-report.

Religiosity, the primary predictor of PD risk was assessed in both ELSA and MIDUS studies by the question: “How important is religion in your [daily] life?” In sensitivity analysis involving the MIDUS data, spirituality was measured as well at baseline with the question: “How important is spirituality in your life?” In that analysis, participants were categorized into three groups: (1) “religion very important”, (2) “spirituality very important but not religion”, and (3) “neither spirituality nor religion very important.” Also collected at baseline in both cohorts was information on religious affiliation (Christian, non-Christian, no religion), frequency of religious/spiritual service attendance, and frequency of private religious practice (prayer and meditation), which were controlled for in analyses. Information on religious upbringing was also assessed in the MIDUS study in 1995–1996 (“How important was religion in your home when you were growing up?”). In a secondary analyses, changes in religiosity prior to baseline in the MIDUS cohort were examined by subtracting scores for religiosity at baseline from scores measured 10 years earlier, creating three categories: religiosity increased, religiosity decreased, and religiosity unchanged.

In addition to religious characteristics, covariates measured at baseline and controlled for in analyses were age, ethnicity, marital status, education, smoking status, alcohol consumption, diabetes, hypertension, mental health conditions, self-rated health, physical activity levels, information on cognitive impairment, and severe mental disorder (ELSA only), and history of serious head injury (MIDUS only). Logistic regression was used to analyze the data. For the primary predictor, “religion very important” served as the reference category, to which other levels of religious importance were compared. Pooled and cohort-specific analyses were conducted. Several types of sensitivity analysis were conducted to confirm the robustness of the findings. Finally, secondary data analysis was conducted on the MIDUS data in order to examine changes in religiosity during the preceding 10 years and risk of incident PD during follow-up.

Otaiku's Findings

With regard to the findings, levels of religious importance in the combined sample were 26.2% for “religion not at all important,” 26.8% for “religion not very important,” 23.4% for “religion somewhat important,” and 23.6% for “religion very important.” The incidence of PD in the combined cohorts during the 8–10 year follow-up was 0.8% ($n=74$). Logistic regression analyses controlling for the covariates above indicated a nearly tenfold increase in risk of developing PD among participants who indicated that religion was not at all important at baseline compared to those indicating religion was very important (OR=9.99, 95% CI=3.28–30.36, $p<0.001$). This effect was found in both the ELSA cohort (OR=6.89, 95% CI=1.48–32.01, $p<0.05$) and the MIDUS cohort (OR=13.69, 95% CI=1.63–114.97). In addition, there was a significant “ p for trend” present overall ($p<0.001$) and in both ELSA ($p=0.006$) and MIDUS datasets ($p=0.003$), indicating a dose–response relationship between decreasing self-rated religiosity and increasing PD risk.

Sensitivity analyses indicated that even after (a) limiting analyses only to those who professed a religious affiliation, and (b) removing religious practices from the model, the findings and dose–effect responses remained robust and statistically significant. In the ELSA cohort, the findings remained significant after excluding PD cases diagnosed within the first two years of follow-up and also after excluding individuals with cognitive impairment or severe mental disorders at baseline. In the MIDUS cohort, the effect strengthened after adjusting for religious upbringing and remained significant after adjusting for serious head injury. After re-categorizing participants based on a combination of religiosity and spirituality, those who considered spirituality but not religion as very important and those indicating that neither spirituality nor religion were very important, were both at increased risk compared to those indicating religion was very important. Finally, in secondary analyses, those whose religiosity during the 10 years preceding baseline had decreased were at more than threefold increased risk of developing PD (OR=3.31, 95% CI=1.16–9.49). The researcher concluded: “This longitudinal study provides evidence for the first time that low religiosity in adulthood may be a strong risk factor for developing PD.”

The Rejoinder

Paal et al.'s rejoinder mentions the following concerns about the Otaiku (2022) study: (1) it is not clear why and how the variables of religiosity and spirituality were combined; (2) it is not reported whether other variables were tested; (3) they refer to the four different groups of how religiosity plays a role, which include extremely small samples of 11, 16, 25, and 22 participants; (4) the final conclusion is based only on the two extreme groups with Parkinson's disease; and (5) it remains unclear whether all patients had Parkinson's disease.

Commentary

In this commentator's opinion, the Otaiku (2022) study was designed well, analyzed appropriately, and presented and interpreted findings accurately, exemplary as state-of-the-art research. There are many positive aspects of this study, including the (a) prospective nature of the data, (b) the fact that two large population-based cohort studies located in different geographical regions of the world were included and long-term follow-up conducted, (c) the extensive control for confounders in multivariate logistic regression analyses, (d) the examination for a gradient of effect (dose–response effect), and (e) the carefully done sensitivity analyses demonstrating consistent findings when examining the data in several different ways. I now examine each of the five concerns that Paal and colleagues raise.

Addressing Paal et al.'s Concerns

(1) *It is not clear why and how the variables of religiosity and spirituality were combined.* First of all, Otaiku made clear that examining the combinations of religiosity and spirituality was not the primary analysis, but rather part of sensitivity analyses designed to determine if the pattern of other data supported the findings of the primary analysis (which it did). Second, and most important, how exactly did Paal and colleagues expect Otaiku to combine religiosity and spirituality in this analysis? There are only four possible categories that could be created by combining the religiosity and spirituality questions: (1) high religiosity and high spirituality; (2) high religiosity and low spirituality; (3) low religiosity and high spirituality; and (4) low religiosity and low spirituality. Otaiku simply combined #1 and #2 into a high religiosity category, so there are no missing data here as Paal et al. claim. Furthermore, this combination of #1 and #2 categories likely increased the number of PD cases for analysis in this combined category. Interestingly, this was one of the concerns of Paal et al. (i.e., not having enough PD cases in each category; see #3 below). Increasing PD case numbers is exactly what Otaiku has done by combining those first two responses into a single category resulting in three not four categories. Furthermore, there is clear precedent for categorizing religiosity and spirituality in this manner, as Otaiku has cited (e.g., Vitorino et al., 2018, and many other studies that could be cited, since this is a common way of measuring combinations of religiosity and spirituality).

(2) *It is not reported whether other variables were tested.* Usually, investigators report all of the variables that were included in an analysis and all statistical tests that were done. It is usually assumed that investigators are being forthright in reporting this information. Criticizing the Otaiku findings due to the mere *possibility* that other variables might have been tested and not reported could be raised for most published studies, and therefore is not a strong argument against the validity of the findings.

(3) *Small number of cases of PD in subcategories.* In describing the four different subgroups of how religiosity plays a role, Paal et al. argue that samples

were extremely small of 11, 16, 25, and 22 participants, potentially invalidating results. They also point out that the final conclusion was based on two extreme groups (11 cases of PD in the very religious group and 22 cases of PD in the not religious at all group, for a total of 33 cases in the analysis overall). This critique, while carrying some merit, in this commentator's opinion does not necessarily invalidate the main findings nor the conclusions from this study (particularly given a dose–response effect in the overall analysis which included all 74 participants).

Prospective cohort studies are commonly published with low event rates, particularly when these events are rare in the population. For example, in a major study of religious attendance and suicide incidence that involve a prospective study of almost 90,000 community-dwelling women published in JAMA and conducted by the Harvard School of Public Health, there were only 36 suicides during the 14-year follow-up (VanderWeele et al., 2016). When distributed across the four categories of religious attendance, suicide events (equivalent to PD cases in the Otaiku study) ranged from 2 to 18. The present distribution of PD cases, while low, far exceeded those numbers.

(4) *The final conclusion is based only on the two extreme groups with Parkinson's disease.* Paal et al. are concerned that the final conclusion was based on a comparison of only the two extreme groups (religion very important vs. religion not at all important). Comparing extreme groups is not at all unusual when investigators want to determine the effect of a particular characteristic on a health outcome. Furthermore, in the current study, a dose–response or gradient of effect was found. This means that at each level of comparison, there was a significant effect and one that was present for every level of religious importance, increasing from a risk of 2.90 (for somewhat vs. very important) to 7.82 (for not very vs. very important) to 9.99 (for not at all vs. very important) ($p < 0.001$). A gradient of effect not only reinforces the findings when comparison of extremes, but also argues for *causality* in the relationship (i.e., that this was not just an association, but possibly an actual causal association going from religious importance to development of PD).

(5) *It remains unclear whether all patients had Parkinson's disease.* Paal and colleagues are correct here in that a physician diagnosis of PD was not determined, but rather PD was determined by self-report. PD is a major medical diagnosis that adversely affects almost every aspect of a person's life. A diagnosis is only given when a neurologist is absolutely certain that this condition is present. Thus, a person's report that they have PD would not likely be a response given lightly or with uncertainty. In the ELSA cohort (which made up nearly three-quarters [73%] of the overall sample), the assessment of PD was done every 2 years over 10 years. It would be highly unlikely that with only a 2-year time interval, that participants would mis-report this diagnosis. The effect in the ELSA cohort was similar to that in the overall sample, including a significant gradient of effect ($p < 0.01$) as noted above.

Biological Mechanism

There is also a plausible physiological mechanism by which religious involvement may reduce the risk of PD, as noted in the Otaiku article. For example, religiosity may support dopaminergic activation through its effects on the vesicular monoamine transporter-2 (VMAT-2), a protein encoded by the SLC18A2 gene (Yulug et al., 2015). Recent neuroimaging has also found that dopamine-rich regions of the brain thought to be involved in PD are also areas of the brain associated with religiosity (Ferguson et al., 2022). Other research shows that high levels of psychological stress may also influence the development of PD by increasing stress hormones such as norepinephrine and cortisol that may accelerate the development of neurodegenerative changes in the brain, as might occur with elevated levels of stress-induced inflammation (Fitzgerald, 2014; Smith et al., 2008). Given the role that religious involvement plays in reducing psychological stress and enhancing well-being (Koenig, 2018), this represents yet another mechanism by which religiosity might reduce the risk of developing PD.

Concern About the Parkinson's Community Reaction

Paal et al. make an important point in stating “We are of opinion that the conclusions of Otaiku’s article could cause anguish and spiritual suffering to many people. Indeed, the paper has caused much controversy and anger in the Parkinson’s community since its publication.” True it might be distressing, but surely it is better for the PD community to be seeking objective empirical evidence that could benefit their loved ones, rather than supporting/advocating for emotional sentiment that potentially hinders the well-being of those with PD. The findings of the Otaiku study in no way indicate that a specific individual with PD is less religious or has less faith than a person without the disease. This common error is frequently and easily made in the application of epidemiologic population research to individual cases and does not do justice to those with this progressive neurodegenerative disorder—one that may actually lead to a deeper faith and greater religious involvement in order to cope with the devastating effects on quality of life caused by this disease (Koenig et al., 2023).

Conclusion

From a scientific standpoint, this commentator would argue that the findings from the Otaiku study indeed represents state-of-the-art research. The finding that greater religiosity may lower the risk of PD cannot be easily dismissed and must be confronted. Paal and colleagues are correct in their conclusion that future studies are warranted in order to replicate the findings reported here. Certainly, this study warrants future research to corroborate these important and potentially far-reaching

findings. However, at least seven other studies with less rigorous design and less statistical analyses than in the Otaiku report have demonstrated an association between PD and low religiosity, as well as work showing that intense religious experiences may improve parkinsonism (all cited in the Otaiku article). Hopefully, the next study will also involve state-of-the-art research design, statistical analysis, and interpretation of results as demonstrated in the Otaiku report.

Funding No funding was provided.

Declarations

Conflict of interest There were no competing interests.

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