

Rocking the boat of vitamin D research in schizophrenia and depression

Henning Tiemeier

COMMENTARY ON... VITAMIN D IN SCHIZOPHRENIA AND DEPRESSION[†]

SUMMARY

A review of studies on vitamin D in schizophrenia and depression found insufficient evidence to inform advice for clinicians. On the basis of the review, I suggest advice for researchers, including better controlling for confounders in observational studies, testing the reverse causality hypothesis, studying vitamin D as a treatment or prevention specifically in patients with more pigmented skin, and prospective community trials of vitamin D supplementation combined with lifestyle advice.

DECLARATION OF INTEREST

None.

KEYWORDS

Depressive disorders; epidemiology; schizophrenia.

schizophrenia and depression (Lally 2019). Several studies reported a cross-sectional association between vitamin D and depression and, to a lesser extent, schizophrenia. However, the authors rightly focus on rigorous longitudinal studies and clinical trials to answer the question whether there is a place for vitamin D supplementation in treatment or prevention of depression and schizophrenia.

Their careful review provides important background information and, although not a systematic review, summarises the seminal studies well. The authors note the paucity of longitudinal data. Further, most of the few prospective studies could not confirm the cross-sectional results. The trials in depression and the single randomised study of schizophrenia were also negative. Hence, evidence is lacking that vitamin D insufficiency is a potential cause of depression or schizophrenia rather than a consequence. The authors point out that the depression trials are limited as they are underpowered, of small sample size and have heterogeneous study populations. They ask again how we should adapt the general population advice for vitamin D use in patients with depression or schizophrenia; they conclude that we do not know and that ‘a presumptive diagnosis of insufficiency could be made, based on risk factors’. Others would argue that the evidence strongly suggests there is no reason to treat these patients differently than other groups at high risk of vitamin D deficiency (McGrath 2017).

Advice for researchers

No advice for clinicians can be given, but what advice should we give clinical or population researchers on the basis of Lally & Gaughran’s review? In view of the poverty of research this is a pressing question and I will try to make some suggestions.

Henning Tiemeier, MD, PhD, is Professor of Social and Behavioral Science and the Sumner and Esther Feldberg Chair of Maternal and Child Health in the Department of Social and Behavioral Sciences, Harvard T. H. Chan School of Public Health, Boston, USA, and Professor of Psychiatric Epidemiology in the Department of Child and Adolescent Psychiatry at Erasmus University Medical Center, Rotterdam, The Netherlands. His research interest is in child developmental cohort studies to unravel the aetiology of common psychiatric problems.

Correspondence Professor Henning Tiemeier, Department of Social and Behavioral Sciences, Harvard T.H. Chan School of Public Health, 677 Huntington Avenue, Boston, MA 02115, USA. Email: tiemeier@hsph.harvard.edu

First received 10 Mar 2019
Accepted 19 Mar 2019

Copyright and usage

© The Royal College of Psychiatrists 2019.

[†]See this issue.

In 1923 Martha May Eliot launched a 3-year prospective trial in New Haven, Connecticut, to determine whether rickets could be prevented by giving infants cod liver oil and teaching mothers to ‘sunbath’ babies even in the winter (Eliot 1925). Her pragmatic community trial was successful because nurses were able to convince mothers of the value of cod liver oil and they even demonstrated how the baby’s mouth was to be held open when administering it. Only 4% in the intervention group, but more than 20% in the control group, developed moderate rickets. This seminal trial not only changed public health practice but also demonstrated that vitamin D requirements differ depending on the infant and that nutritional interventions can best be combined with lifestyle changes (Hunt 1995).

The Lally & Gaughran review

In this edition of *BJPsych Advances*, Lally & Gaughran review studies on vitamin D in

First, the research reflects insufficiently that vitamin D has been implicated in an indefinite number of acute and chronic conditions. Low vitamin D levels seem a frailty indicator or a biomarker of a poor health status at times. Depression and schizophrenia certainly occur often as a direct or indirect consequence of disorders that have been related to vitamin D. This means that observational studies must control much more carefully for confounding by disease and, importantly, by subclinical traits. This should resolve some of the discrepancies between studies. Against this background, the studies reviewed by Lally & Gaughran that specifically look at vitamin D and bone mineral density only in psychosis are probably not the way forward; it is unclear why this particular relation should differ in psychiatric patients. Rather, carefully controlled longitudinal studies of multiple morbidities accounting for competing risks are needed.

Second, Lally & Gaughran mention that people with more pigmented skin have a higher rate of psychosis and lower vitamin D levels when living in northern or southern countries than those with less pigmented skin. In particular, persons from Black African or Caribbean ethnicity are affected. Vitamin D treatment or prevention studies in darker-skinned populations are called for (Dealberto 2007; McGrath 2011).

Third, reverse causality, as Lally & Gaughran point out, is a likely explanation for the discrepancy

between cross-sectional and longitudinal studies. Why does nobody test this explanation? With repeated measures of vitamin D, it would be easy to examine whether depression or schizophrenia lead to changes in vitamin D levels owing, for example, to less outdoor activity.

Finally, and most importantly, we need another Martha May Eliot to rock the boat of the small cross-sectional clinical vitamin D studies currently performed in psychiatry. We need another pragmatic and prospective community trial of vitamin D supplementation combined with lifestyle advice. Like the mothers of young children, persons with low levels of vitamin D at high risk of depression and psychosis may need to be taught how to effectively exercise, sunbathe and eat healthily.

References

- Dealberto MJ (2007) Why are immigrants at increased risk for psychosis? Vitamin D insufficiency, epigenetic mechanisms, or both? *Medical Hypotheses*, **68**: 259–67.
- Eliot MM (1925) The control of rickets: preliminary discussion of the demonstration in New Haven. *JAMA*, **85**: 656–63.
- Hunt M (1995) 'Extraordinarily interesting and happy years': Martha M. Eliot and pediatrics at Yale, 1921-1935. *Yale Journal of Biology and Medicine*, **68**: 159–70.
- Lally J, Gaughran F (2019) Vitamin D in schizophrenia and depression: a clinical review. *BJPsych Advances*, this issue.
- McGrath JJ (2011) Migrant status, vitamin D and risk of schizophrenia. *Psychological Medicine*, **41**: 892–5.
- McGrath JJ (2017) Vitamin D and mental health – the scrutiny of science delivers a sober message. *Acta Psychiatrica Scandinavica*, **135**: 183–4.