may be regarded as an indicator of altered neuroplasticity in depression, reflecting prolonged susceptibility of depressed individuals towards uncontrollable stress. This process can apparently be reversed in the context of clinical improvement.

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Declaration of Interest

None.

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Letter to the Editor

Migrant status, vitamin D and risk of schizophrenia

Bourque and colleagues have provided a useful update of the evidence linking migrant status and risk of schizophrenia (Bourque *et al*. 2010). The evidence is convincing. What remains for the research community is to generate biologically plausible mechanisms that may underpin this increased risk. Previously, we proposed that low prenatal vitamin D might be a risk factor contributing to the increased risk of schizophrenia in certain migrant groups (McGrath, 1999). Bourque *et al*. note in their review that this hypothesis might account for part of the increased risk, but suggest that this candidate 'could scarcely account for the higher risk among lighter-skinned immigrants in some contexts (e.g. Moroccans in The Netherlands) or other groups who moved to warmer climates'.

In fact, there is abundant evidence showing that 'lighter-skinned immigrants' such as the Moroccans in the Netherlands are at increased risk of hypovitaminosis D. A detailed systematic review has recently been published on this topic (van der Meer *et al*. 2010). With respect to the relative difference in this exposure between different migrant groups, a population-based study of German children and adolescents ($n = 10\,015$) has provided informative relative risks (Hintzpeter *et al*. 2008). Compared with non-immigrants, those from Africa have the highest adjusted odds ratio for vitamin D deficiency (about seven-fold), followed by migrants from Arab-Islamic countries (about six-fold) and Turkey (about four-fold) (Hintzpeter *et al*. 2008). Apart from darker skin colour, variables related to dress (e.g. wearing a veil), behaviour (e.g. less outdoor activities) and diet also contribute to an increased risk of vitamin D deficiency in certain minority groups, regardless of skin colour or ethnicity (Rejnmark *et al*. 2004; Holick, 2007; Lips, 2010). Of course, you do not need to be a migrant to have low vitamin D deficiency and insufficiency are prevalent in many nations (Mithal *et al*. 2009).

The original vitamin D hypothesis focused exclusively on prenatal exposures. Animal experiments

demonstrate that transient prenatal hypovitaminosis D is associated with persisting changes in brain structure and function, including convergent evidence of altered dopaminergic function (McGrath *et al*. in press). Thus, the hypothesis might account for the second-generation migrants who are at increased risk of developmental vitamin D deficiency, but it cannot explain the first generation migrants who arrive as children or adults. In recent years new evidence has accumulated showing that vitamin D has neuroprotective properties in the post-natal brain (McCann & Ames, 2008). Thus, it is feasible that chronic hypovitaminosis D could leave individuals more vulnerable to subsequent neurobiological insults. For example, migrant groups exposed to both 'social defeat' (Selten & Cantor-Graae, 2005) and hypovitaminosis D may be less able to buffer neurotoxicity related to stress-related mechanisms (Obradovic *et al*. 2006).

Because vitamin D is safe, cheap, acceptable to the general public, and could help a range of physical health outcomes other than schizophrenia, there is a public health case to undertake exploratory trials of vitamin D in groups at risk of hypovitaminosis D promptly (McGrath, 2010).

Declaration of Interest

None.

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The authors reply

We are grateful to John McGrath for his useful literature update and eloquent elaboration on the potential role of vitamin D deficiency in the onset of schizophrenia and related disorders among immigrants.

There is indeed a need to investigate biologically plausible mechanisms that may underlie the excessive incidence of psychotic disorders among migrant and ethnic minority groups. Insights gained from such knowledge may shed light on the onset of psychosis, not only among migrants, but in the general population. Also, any plausible and reasonably testable hypothesis deserves further consideration from the scientific community if it may help us address what has been appropriately termed as 'a public health tragedy' (Morgan & Hutchinson, 2010). One of the most appealing aspects of the vitamin D deficiency hypothesis is that it may be potentially correctable, as highlighted in McGrath's letter.

Although this research avenue may be promising, we would caution against being overly optimistic in explaining the migration and psychosis conundrum based on any single hypothesis. For instance, there are a number of questions that remain unaddressed with the vitamin D hypothesis as currently proposed. Our findings suggest that putative explanatory models should ideally account for the increased risk of psychotic disorders among both first and second generations of immigrants. As acknowledged in the letter, if the increased liability for psychotic disorders among immigrants resulted primarily from a peri-natal or early-life exposure to hypovitaminosis D, it is unclear how this could account for the risk among first-generation immigrants – who appear at higher risk even though they migrated in adulthood. Given the relatively early onset of psychotic disorders (with a peak around 22 years old), there would be only limited exposure to the putative risk factor following immigration. Further evidence on the relationship between age at migration and the risk of psychosis may eventually provide further clues in this respect.

Further considerations include the need to account for increased incidence rates not only among prevailing groups migrating to latitudes less exposed to sunlight, but also among others who moved to similar or even warmer climates (e.g. Finns in Sweden, Russians in Israel or Greenlanders in Denmark). In addition, Asian immigrants in the UK appear to present higher rates of hypovitaminosis D, yet without the substantially higher risk of psychosis observed in immigrants of Caribbean origin (Morgan *et al*. 2010). Without implying causality, it is at least a significant source of concern that the latter group is reportedly the most likely to report instances of racial harassment or discrimination (Karlsen *et al*. 2005).

Our review has highlighted considerable variation in the magnitude of the risk across countries, but also within countries (Bourque *et al*. 2010). For instance, in The Netherlands, there seems to be a gradient whereby Moroccan immigrants present the highest risk for psychosis, followed by those of Surinamese origin, and lastly those of Turkish origin. It is rather intriguing that the degree of perceived discrimination appears to follow a similar pattern (Veling *et al*. 2007). But perhaps even more striking are the replicated findings of a 'neighbourhood ethnic density' phenomenon, whereby the risk of migrant and ethnic minority groups appears to increase as they comprise a lower proportion of the neighbourhood population, in a seemingly dose–response fashion (Boydell *et al*. 2001; Kirkbride *et al*. 2007; Veling *et al*. 2008). Such patterns of risk defy strictly biological explanations, and indicate that the broader social environment must be considered as we attempt to understand the relationship between migrant status and the risk for psychotic disorders.

Morgan *et al*. (2010) have recently suggested a socio-developmental model in an attempt to integrate the expanding evidence for social determinants with the existing knowledge on genetic and neurodevelopmental pathways to psychosis risk factors. It is possible that hypotheses such as vitamin D deficiency (McGrath, 1999; Dealberto, 2007) or social defeat (Selten & Cantor-Graae, 2005) may both operate within such a model. Epigenetic mechanisms represent another promising area that may reconcile genetic, biological and socio-environmental risk factors (Peedicayil, 2008), as they represent a plausible model according to which various environmental exposures – including adverse social experiences – may translate into differential gene expression.

While some biological risk factors may be reliably measured through blood samples, socio-environmental exposures may not be yet readily identifiable or reliably measured with prevailing psychiatric research methods. McGrath has recently argued that shared research endeavours and cross-disciplinary exchanges between schizophrenia epidemiology and basic neuroscience would be of much benefit to both fields (McGrath & Richards, 2009). We are very much in agreement with this statement, but we would like to add that there is also a call to better integrate the knowledge and approaches of social sciences if the scientific community is to make significant advances in the complex relationship between migration, ethnicity and psychosis, a public health problem which has lagged behind for too long at the expense of vulnerable populations.

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