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Letter to the Editor

Congenital blindness is protective for schizophrenia and other psychotic illness. A whole-population study.

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1. Introduction

While visual impairments appear to be a risk factor for schizophrenia (Adams and Nasrallah, 2018; Silverstein and Rosen, 2015; Torrey and Yolken, 2017), since the 1950s it has been observed that congenital and early blindness may be protective (Chevigny and Braverman, 1950). This proposal has been supported by a number of more recent case studies and reviews (Landgraf and Osterheider, 2013; Leivada and Boeckx, 2014; Silverstein et al., 2013). The protection possibly extends to psychotic disorders in general (Leivada, 2016) but not to other mental illness (Silverstein et al., 2013). Two kinds of congenital blindness have been distinguished: peripheral blindness arising in the globe and cortical blindness arising from lesions in the occipital cortex. Critically, it has been suggested that the protective effect is restricted to cortical blindness, not peripheral blindness (Leivada, 2016; Leivada and Boeckx, 2014).

The reliability of this differential protection is important for understanding the aetiology of psychosis. Yet, we are aware of no whole-population studies examining this phenomenon. Our main aim was to use Western Australian State-wide registers to estimate the distribution of cases of schizophrenia among people with congenital and early blindness, examining separately exposure to cortical and peripheral blindness. We hypothesised that congenital and early cortical but not peripheral blindness would be protective against schizophrenia. A secondary aim was to repeat the analyses for the broader diagnostic outcome, psychotic illness.

2. Methods

This study utilises linkages across administrative health registers, facilitated via the Western Australian Data Linkage System, to build on a broader program of work investigating risk factors for psychotic illness in a cohort of almost 500,000 individuals born in Western Australia between 1980 and 2001. Full details on the cohort and Western Australian whole-population databases and registries have been published (Morgan et al., 2011).

Psychiatric data for the cohort came from hospital separations records on the Hospital Morbidity Data Collection and outpatient/community mental health contacts on the Mental Health Information System. Data were extracted in June 2015, when the cohort was aged between 14 and 35 years. *Schizophrenia* was recorded if there was any history of a diagnosis of schizophrenia (ICD-9 295.xx). A *psychotic illness* was recorded if there was any history of schizophrenia, affective psychoses, paranoid states and other nonorganic psychoses (ICD-9 295.xx-298.xx). ICD-10 codes were mapped to ICD-9.

The following databases were searched to identify cases of cortical and peripheral blindness: Midwives Notification System (mandatory reporting of births at 20 weeks gestation or greater or weighing at least 400 g, including home births); Birth Defects Registry (mandatory reporting of defects occurring up to the age of 6 years); Hospital Morbidity Data Collection (mandatory recording of all hospital admissions). Only children aged 6 years or under at time of diagnosis were included, the same age threshold for early blindness recommended by Leivada and Boeckx (2014) based on previous literature. Conditions selected for cortical blindness were: cortical blindness; retinal dystrophy; blindness in both eyes; and malignant neoplasm involving bilateral enucleation. Conditions selected for peripheral blindness were: congenital glaucoma; congenital lens malformations; and retrolentical fibroplasia. The actual codes used varied according to the classification system in the data source and are available on request.

3. Results

In our cohort of 467,945 children aged between 14 and 35 years at time of psychiatric data extraction, 1870 children had developed schizophrenia (0.4%) while 9120 had developed a psychotic illness including schizophrenia (1.9%).

There were 66 children with cortical blindness (1.4 per 10,000): 60.6% were male and 12.1% were Indigenous; six had at least one parent with a psychotic illness. None of the children with cortical blindness had gone on to develop schizophrenia, nor any other psychotic illness. There were 613 children with peripheral blindness (13.1 per 10,000): 51.2% were male and 11.4% were Indigenous; 39 had at least one parent with a psychotic illness. Eight of the 613 children with peripheral blindness had developed a psychotic illness other than schizophrenia, all of which were affective psychoses in the ICD-9 296 range, and fewer had developed schizophrenia; 90 children had developed another mental illness. See Table 1.

4. Discussion

The results from this whole-population cohort, although possibly underpowered, lend confidence to findings from smaller case studies that congenital or early cortical but not peripheral blindness is protective against schizophrenia. While median lifetime morbid risk for schizophrenia is estimated to be 0.72% (Saha et al., 2005), many of our young cohort had still not passed through the window for schizophrenia onset. Using the age distribution of our cohort, as well as age-of-onset data from the 2010 nationally representative Australian survey of psychotic illness (Morgan et al., 2012), we estimate that 0.5% of a

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Table 1
Type of blindness and co-occurring schizophrenia/psychotic illness (N).

	Congenital/early blindness	Schizophrenia	Psychotic illness other than schizophrenia
	N	N	N
Cortical blindness	66	0	0
Peripheral blindness	613	<5[a]	8

[a] Small cell size with N < 5 therefore not publishable.

population cohort aged 14–35 would have developed schizophrenia, similar to the estimate of 0.4% for the total cohort that we report here. In our data, this dropped to 0.2% for congenital or early peripheral blindness and was zero for congenital or early cortical blindness. Our data further suggest that the protection offered by cortical blindness may extend to a broader range of psychotic disorders and that risk of psychosis may effectively be reduced to zero.

The underlying mechanism by which congenital and early blindness confer protection requires further elucidation. Silverstein et al. (Silverstein et al., 2013) propose that a cluster of perceptual and cognitive functions that are impaired in schizophrenia are enhanced in those with congenital and early blindness compared to normal sighted individuals; this includes auditory perception, auditory attention, memory, language and the construction of subjective experience. It appears that early compensatory developmental neuroplasticity (for example, via cortical reorganisation and changes affecting the occipital region) creates advantages for blind people in the very functions that are impaired in schizophrenia. Similarly, Landgraf and Osterheider demonstrate compensatory neurofunctional and multisensory reorganisation in congenitally blind people in a more complex continuous model (the "Protection-Against-Schizophrenia" hypothesis) that grades severity of blindness/visual impairment and severity of psychosis (Landgraf and Osterheider, 2013).

Why then would this effect be observed with cortical but not peripheral blindness? Leivada and Boeckx (2014) suggest that both congenital cortical and peripheral blindness may afford some protection against schizophrenia. But, as Silverstein et al. note, different forms of blindness affect different structures involved in the visual system (Silverstein and Rosen, 2015), and Leivada and Boeckx postulate that the observed, apparently complete, protection seen with congenital cortical blindness may be due to differentially impaired connectivity (and related linguistic and cognitive operations) between brain areas, with subcortical, thalamic structures remaining largely intact in congenital cortical but not peripheral blindness.

This study benefited from access to large mandated databases with state-wide coverage of prospectively collected data. However, there are several limitations. First, there may have been some under-ascertainment of schizophrenia cases since the psychiatric registers do not include data on visits to general practitioners and private psychiatrists/psychologists. In addition, the children were aged between 14 and 35 years when their psychiatric histories were extracted; it is likely that, as the cohort ages, more incident cases of schizophrenia will arise, especially among the younger cohort members. Second, the inability to access records in general practices may also have led to under-ascertainment of blindness in the children, particularly early blindness. Finally, for some forms of peripheral blindness, it was not possible to know from the records available to us whether the condition had been corrected after it had been identified.

The protective phenomenon observed in case studies of people with congenital cortical blindness, and now supported by our whole-population data, warrants careful, clinical investigation. Determining the underlying biomechanisms will enhance our understanding of the complex aetiology of schizophrenia. Moreover, it offers hope of identifying potential targets for early intervention and prevention in schizophrenia, including therapeutic strategies directed at the reorganisation of cortical functioning (Landgraf and Osterheider, 2013) and early cognitive training with an emphasis on sensory-perceptual functioning (Silverstein et al., 2013).

Declaration of interest

The authors have no conflicts of interest to declare in relation to this work.

Author contributions

AJ and VM developed the idea for the study. All authors contributed to the study protocol. MC, JC, GV, DM and VM contributed to data coding and analysis. VM undertook the literature searches and wrote the first draft of the manuscript. All authors contributed to subsequent drafts and have approved the final manuscript.

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This study was approved by the Western Australian Department of Health Human Research Ethics Committee (2011/75) and The University of Western Australia Human Research Ethics Committee (RA/4/1/1322).

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