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Environmental factors and the age at onset in first episode psychosis

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ABSTRACT

Objective: Factors that influence the age at onset in psychotic disorders could provide valuable insights into precipitating or causative factors of the disorder. Despite being established risk factors, it is not yet known whether migration status, place of birth, social class at birth and season of birth influence the age at onset of psychotic disorders. This study aimed to determine whether these environmental factors, in addition to cannabis abuse and obstetric complications, influence the age at onset. Additionally, we investigated whether environmental factors could have a cumulative effect on the age at onset.

Method: Data was obtained from two first episode of psychosis (FEP) cohort studies. Diagnosis was established using the Structured Clinical Interview for DSM IV diagnoses.

Results: The age at onset was determined for 555 individuals with a FEP and the median age at onset was 27.3 years. Individuals with a history of cannabis abuse had an earlier age at onset by nearly six years. There was a trend for a history of obstetric complications to be associated with a younger age at onset by 2.7 years and this was significant in the subgroup with a family history of psychosis. Social class at birth, migration status, place of birth and season of birth were not associated with the age at onset. Exposure to a higher number of environmental factors was associated with an earlier age at onset.

Conclusions: Cannabis and obstetric complications are associated with an earlier age at onset and there appears to be a cumulative effect of exposure to multiple environmental factors.

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1. Introduction

The aetiology of psychosis is not yet fully understood however factors that influence the age at onset of psychotic disorders could provide valuable insights into precipitating factors or the causation of the disorder. The age at onset has been described as 'the single most important characteristic of schizophrenia that could yield clues to its origin' (DeLisi, 1992). A number of demographic and clinical characteristics have been consistently associated with an earlier age at onset of psychotic disorders, such as male gender (Castle et al., 1998; Faraone et al., 1994), a family history of a psychotic disorder (Esterberg et al., 2010), obstetric complications (Verdoux et al., 1997) and cannabis use (Large et al., 2011). Surprisingly, there has been a dearth of research

into the influence on the age at onset of psychosis for other established environmental risk factors, such as migration, season of birth, social class and place of birth. The limited studies to date have suggested that migration and the season of birth are not associated with the age at onset (Scherr et al., 2012; van der Ven et al., 2012). While not specifically examining the age at onset, Mulvany et al. demonstrated that individuals with a FEP from a higher social class at birth presented to the mental health services eight years younger than those from a lower social class at birth (Mulvany et al., 2001).

Stepniak et al. (2014) examined the influence of environmental factors on the age at onset in a cohort of 750 males with a diagnosis of either schizophrenia or schizophreniform disorder (Stepniak et al., 2014). The study found that perinatal complications, neurotrauma and cannabis use before the age of eighteen were strong predictors of an earlier age at onset, while individually, psychotrauma, urbanicity and migration were not. Yet, exposure to multiple environmental factors had a cumulative effect and individuals exposed to four of these factors had an earlier age at onset by over a decade. This indicated that some environmental factors may not individually influence the age at onset however collectively they could have an effect. However this study was confined

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to males only and it is not clear whether this association is also present for females and all first episode diagnoses.

Understanding the factors that influence the age at onset may not just deliver insights into the aetiology of psychotic disorders but could also enable early intervention services to tailor the service to the demographics and clinical characteristics of those developing a psychotic disorder.

Therefore, this study aimed to determine if the age at onset of psychotic disorders was associated with environmental factors, specifically: social class at birth, place of birth, season of birth, migration, obstetric complications and cannabis use, while controlling for gender, family history of psychosis and diagnosis. Second, it aimed to determine whether there was a cumulative effect of these environmental factors on the age at onset.

2. Materials and methods

2.1. Participants & setting

Two cohorts were included in this study, the first consisting of individuals with a FEP who presented to an urban catchment area community mental health service (population 165,000) between 1995 and 1999. Findings from this cohort, other than on the age at onset, have been published elsewhere (Clarke et al., 2006; Crumlish et al., 2009). The second epidemiological cohort consisted of individuals with a FEP who presented to the abovementioned catchment area and two adjacent catchment area mental health services (total population 360,000) between February 2006 and August 2011.

A FEP was defined as fulfilling the criteria for a psychotic disorder according to the Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders IV (SCID). This equated to an individual having full threshold psychotic symptoms for a period of at least one week and having no previous history of a psychotic episode and not having received antipsychotic medication for more than thirty days prior to the referral.

2.2. Instruments

All individuals underwent a Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders IV (SCID) assessment to confirm the diagnosis of a first episode of psychosis, an instrument that has shown good reliability and validity in the assessment of psychotic disorders (First et al., 2002). The SCID assessment was also used to determine the presence of cannabis abuse.

The onset of psychosis prodrome and the onset of full threshold psychotic symptoms were established using the Beiser Scale and this resulted in an estimation of the duration of untreated psychosis (DUP) (Beiser et al., 1993). The DUP was recorded in months and it was defined as the length of time between the onset of prominent psychotic symptoms and the date of first presentation for treatment. The Beiser Scale was completed by interviews with families and this information was augmented with the information gained from the interviews with participants. The age at onset was calculated by subtracting the DUP from the age at presentation.

The Lewis and Murray Obstetric Complications Scale (MLOCS) was used to detect the presence of any of fifteen possible obstetric complications and this instrument was used in the interview with the participant's mother (Lewis et al., 1989). The MLOCS includes such obstetric complications as caesarean section, premature rupture of membranes, forceps delivery, breech birth, labour shorter than 3 h and foetal distress. The MLOCS codes each complication as either present or absent. Three different analyses were conducted in regards to the association between obstetric complications and age at onset. First, it was investigated whether the age of onset differed according to the presence of each individual obstetric complication. Second, it was investigated whether obstetric complications as a collective group, with a

dichotomous variable of either 'any obstetric complication' or 'no obstetric complications' was associated with the age at onset. Third, it was determined whether there was a dose–response relationship between obstetric complications and the age at onset. The MLOCS was only conducted in the second cohort.

2.3. Sources of information

Information relating to the social class at birth, season of birth and place of birth was obtained from the participant's birth record. Social class at birth was determined from the father's occupation as recorded on the individuals' birth certificate and each occupation was coded according to the Republic of Ireland Census Classification (Central Statistics Office, 2011). There are six social classes that are broadly defined as social class I – professional workers, social class II – managerial and technical, social class III – non-manual, social class IV – skilled manual, social class V – semi-skilled and social class VI – unskilled. A dichotomous variable of social class was also created and social classes I–III were grouped together as the 'higher social class' and social classes IV–VI were grouped together as the 'lower social class'.

The Irish Central Statistics Office (CSO) divided the country of Ireland into eight strata according to the level of population density and the definition of 'urban' and 'rural' was taken from this classification (Central Statistics Office of Ireland, 2006).

2.4. Ethical approval

Ethical approval for the study was obtained from the governing ethics committees of the three community mental health services, specifically the St. John of God Hospitaller Service ethics committee, St. Vincents University Hospital and Newcastle Mental Health Services.

2.5. Statistical analysis

Data were analysed using PASW Statistics 18. Mann–Whitney U tests were performed to determine if there was a difference in the median age at onsets for variables. When there was a significant difference or a trend, a dichotomous variable of 'earlier and later age at onset' was created from the median value of the age at onset, consistent with the method utilized by Verdoux et al. (1997). This additional analysis permitted the production of odds ratios that have a clinically meaningful interpretation. The Kruskal–Wallis one-way analysis of variance was used for more than two continuous, non-parametric variables. Spearman's rho correlation coefficient was used to determine if non-parametric data were correlated. Binary logistic regression was conducted to control for potential confounding between variables; due to missing data pertaining to obstetric complications, this variable was excluded from the logistic regression model. We performed analysis on sub-groups and we stratified groups according to gender, family history of a psychotic disorder and diagnosis (non-affective FEP vs affective FEP). Participants were only counted as having the exposure of either cannabis abuse or migrant status if these factors preceded the onset of the psychotic disorder.

A cumulative exposure score was created and corresponded to the total number of environmental factors to which each individual was exposed. As there was limited data on the presence of obstetric complications, one model included the variable on obstetric complications and another model included the other variables but excluded the obstetric complications variable. Information relating to the social class at birth was only available for individuals born in Ireland and was not available for migrants. Therefore, for each of the above sets of analyses, one model that included social class at birth but not migrant status was performed and then a second model that included migrant status but not the social class at birth was performed. Jonckheere's trend test was performed to determine whether the age of onset differed according to the accumulated number of exposures to environmental factors. This test was

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