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Evidence that better outcome of psychosis in women is reversed with increasing age of onset: A population-based 5-year follow-up study

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ABSTRACT

Background: Female gender and later onset of psychosis are both associated with better outcome. However whether their effects are independent, is not known.
Method: In 379 incident cases of psychoses, from an epidemiologically defined catchment area, admixture analysis was employed to generate age of onset classes. Five year course and outcome measured across clinical and social domains were used as dependent variables in regression analyses, to estimate associations of outcomes with gender, age of onset and gender by age of onset interaction.
Results: Three age of onset classes were identified: early (14–41 years), late (42–64 years) and very late onset psychosis (65–94 years). Overall, women had better outcomes, including milder delusions, fewer negative symptoms, less deterioration from baseline functioning, fewer hospital readmissions and shorter psychotic episodes. Later age of onset was also associated with better outcome, although in the very late onset class the results were mixed. There was a statistically significant gender by age of onset interaction (in the ratio scale) within this sample with men displaying poorer outcome in the early/late onset class, whereas women tended to have a worse outcome in the very late onset class.
Conclusions: The favourable outcome in women becomes reversed in old age, suggesting gender-age-related differences in the distribution of aetiological factors for psychosis.

1. Introduction

Psychotic disorders show significant variation in their clinical presentation, course and outcome, probably reflecting aetiological and pathophysiological heterogeneity (Andreasen, 1995). Studying outcome can help elucidate the causes of such heterogeneity (Kendell, 1989; Robins and Guze, 1970). Several published studies suggest women have a better prognosis, including better global and psychosocial functioning, a less chronic course, fewer re-hospitalizations, shorter inpatients stays, reduced negative symptoms and significantly less disability (Goldstein, 1988; Leung and Chue, 2000). Furthermore, other putative differences have been reported such as fewer obstetric complications, less structural brain changes, less severe negative symptoms, more affective symptoms and better premorbid functioning in women (Leung and Chue, 2000). These differences suggest the distribution of aetiological factors may vary between the genders (Castle et al., 1995).

Yet the most consistent finding regarding gender differences in psychosis is the later age of onset in women and

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female overrepresentation in later onset samples (Angermeyer and Kuhn, 1988; Howard et al., 2000). As later age of onset is also associated with better outcome in schizophrenia and other psychoses (Haro et al., 1994; Malla et al., 2006; Rabinowitz et al., 2006), it can be hypothesised that gender and age of onset are not independent predictors of outcome.

The present study therefore reports the 5-year outcome, in a population of patients with first-episode psychoses, across the full adult age-range, and examines the effects of gender and age of onset (and their statistical interaction) on multiple clinical and social domains of outcome, while adjusting for factors known to potentially influence outcome, namely a positive family history for schizophrenia, a diagnosis of schizophrenia (as opposed to other psychoses), baseline symptoms and marital status (van Os et al., 1997).

2. Method

2.1. Participants

Case ascertainment has been described elsewhere (Allardyce et al., 2000). Briefly, all first contacts with an ICD-9 or ICD-10 diagnosis of schizophrenia, schizoaffective disorder, delusional disorder, mania, drug-induced psychotic disorder and acute, transient or unspecified psychotic disorder presenting to the psychiatric service (inpatients, day patients, outpatients, domiciliary assessments and informal out-of-hour contacts) of Dumfries and Galloway (D&G) between the years 1979 and 1998 were identified. Exclusions criteria were: no resident of D&G, psychotic symptoms prior to the study period, organic psychosis. This left a cohort of 464 patients for inclusion.

2.2. Baseline assessment

Demographic characteristics and the absence or presence of symptoms were extracted from the case records and ancillary documentation. Two experienced psychiatrists (JA, GM) completed The Operational Checklist for Psychotic Disorders (OPCRIT) (McGuffin et al., 1991). Good inter-rater agreement for both 1) individual symptom measures (kappa = .69–.92) and 2) DSM-IV diagnoses generated using OPCRIT 3.4 algorithm (kappa = .79) have been demonstrated (Allardyce et al., 2000). Age of onset was defined as age of first contact with psychiatric service. As described previously (Allardyce et al., 2007), an exploratory factor analysis of first year OPCRIT ratings identified five latent symptom dimensions, explaining 58% of the variance: mania, depression, disorganization, hallucinations, delusions. Factor scores were calculated for each individual for the five dimensions.

2.3. Outcome measures

The Local Regional Ethics Committee and the Privacy Committee of Information and Statistical Division in Scotland approved the follow-up study. Patients were traced between the years 2004 and 2005 using medical, regional and nationwide registers. Four-hundred-and-twenty-two (91%) patients were traced (median time from presentation to follow-up = 11.82 years, inter-quartile-range = 6.67–18.41). Where possible, multiple sources of information were used (systematic review of case notes, patient interviews, information from health professionals involved in day-to-day patient care and family members). All staff were formally trained and participated in regular review meetings and exercises from recorded interviews. Five-year outcome measures were created using items from the OPCRIT, WHO Life Chart Schedule (LCS) (World Health Organization, 1992) and Life Time Dimensions of Psychosis Scale (LTDS) (Levinson et al., 2002). The LCS was rated by research workers demonstrating good reliability (pairwise agreement >0.8 for all items used in the analyses) and the LTDS was completed by a single rater (JA). Outcomes included severity of delusions and hallucinations (both: 0 = mild/moderate, 1 = severe), presence of formal thought disorder, negative symptoms, first rank symptoms of Schneider and functional deterioration from levels at baseline/first admission (all: 0 = absent, 1 = present), course type (1 = one episode, 2 = multiple episodes, 3 = continuous symptoms), type of remission (1 = none, 2 = residual, 3 = complete), number of readmissions (1–5 or more), time of longest psychotic episode (in months), and time spent in supported residences (in months). The variables *longest psychotic episode* and *time spent in supported residency* suggested a skewed distribution. Therefore categories based on tertile cut-offs were generated and used in the analyses.

2.4. Statistical analysis

2.4.1. Admixture analysis of age of onset

Rather than using arbitrary age cut-offs to construct age of onset subgroups, we used admixture analysis in Mplus 4.0 (Muthen and Muthen, 2006). This method examines whether the observed continuous age of onset distribution could be better modelled as a mixture of two or more Gaussian distributions (McLachlan and Peel, 2000). It starts with the most parsimonious single-Gaussian distribution model and fits successive models with increasing numbers of distributions. Whether the model with $n+1$ distributions fits the observed distribution better than the model with only n distributions was compared using several model fit indices: 1) adjusted Lo–Mendell–Rubin likelihood ratio test (LRT) (Lo et al., 2001) 2) Akaike's information criterion (AIC) (Akaike, 1987) 3) Bayesian information criterion (BIC) (Schwartz, 1978). Subjects can then be classified into age of onset subgroups identified by the different underlying distributions. How well this classification fits the data is measured using standardised entropy scores (Ramaswamy et al., 1993).

2.4.2. Missing outcome data

Missing values are almost inevitable in epidemiological studies but most follow up studies ignore possible bias introduced by analyzing cases with complete information only. To deal with the missing data we used multiple imputation methods which assume data is missing at random (MAR) (Rubin, 1976). The method imputes several alternative versions of the complete dataset using the data that was not missing. These are then analyzed separately and the effect sizes and standard errors, which may vary, are combined using simple arithmetical procedures to obtain overall estimates. For follow-up measures with missing values, other than death, we imputed 20 datasets in STATA 9.2 (StataCorp, 2006) using the