Clinical Predictors of Treatment-Resistant Schizophrenia

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Abstract

Objective: To identify clinical and demographic factors associated with treatment-resistant schizophrenia (TRS).

Method: We present 147 cases with TRS and 135 without TRS. Logistic regression was conducted to test for association with family and background factors, premorbid functioning and illness presentation with TRS in a univariate analysis, and significant variables were entered into a multivariate model.

Results: Age of onset of psychosis (p=.002) and age of first antipsychotic treatment (p=0.000) were significantly associated with TRS. Age of first treatment remained significant (p=0.027) in a multivariate model. Younger age at first treatment for psychosis is a risk factor for TRS.

Background

Around 30% of people with schizophrenia fail to respond to initial antipsychotic treatment. Patients with treatment resistant schizophrenia (TRS) typically report poor levels of functioning and quality of life. Clinicians are currently unable to identify which patients will be treatment resistant when they first present with psychosis. A proven and recommended treatment for TRS is the antipsychotic clozapine (NICE guidelines). Despite its proven efficacy, research has demonstrated significant delays before TRS patients receive clozapine, and that such delays are associated with poorer outcome. It is therefore important for TRS patients to be identified and receive clozapine as early as possible during the course of their treatment. Factors indicating TRS could improve the ability of clinicians to further monitor and support those more likely to develop TRS, determine at an earlier stage which patients will require clozapine, or potentially prevent the illness progressing to this stage.

We hope to contribute to the development of predictive algorithms for TRS.

Sample

The sample was obtained from the Cardiff Cognition in Schizophrenia (Cardiff COGS) sample, a locally recruited sample of patients with psychosis and schizophrenia from South Wales. All participants complete a clinical research interview (SCAN), had symptom and diagnosis ratings and a consensus rating of symptoms and diagnosis. A questionnaire exploring experiences of antipsychotic medication was sent to 605 participants for whom we had valid contact details. Questionnaire data was collected for 372 participants (62% response rate). Of those who responded we had interview and ratings data available for 282 participants.

Data from the questionnaire was used to define TRS in our sample.

Treatment-resistant schizophrenia (N=147):
(i) Ever taken clozapine, or (ii) taken >2 antipsychotics but report current medication is helping.

Non treatment-resistant schizophrenia (N=135):
(i) Taken ≤2 antipsychotics, or (ii) taken >2 antipsychotics but self report current medication is not helping.

Clinical/demographic predictors

Predictor variables were derived from the Cardiff COGS interview and based on those that would be helpful to clinicians when identifying patients present with psychosis/those not subject to illness or treatment confounds. Predictor variables were placed into three subgroups:

1. Family and background factors: Sex, main place of upbringing, family history of schizophrenia, family history of other psychiatric disorder, mother’s age at birth, father’s age at birth, and childhood sexual or alcohol abuse as measured by the CLEQ.

2. Premorbid functioning:
Birth complications, pregnancy complications, development problems, years in education, full IQ estimated from NART score, and premorbid adjustment as measured by the combined PMAS score at 6-12yrs and 13-21yrs.

3. Illness presentation:
Age of onset of psychosis, age of first antipsychotic treatment, duration of untreated psychosis, and alcohol and drug use within one year of onset.

Analysis

A logistic regression to test for association with TRS was conducted using SPSS. Predictor variables were first analysed in a univariate model, and significant variables were entered into a multivariate model. In order to account for multiple testing, the Bonferroni correction method was applied to each subgroup.

Significant variables from the univariate model were entered into a multivariate model. Age of first antipsychotic treatment, but not age of onset of psychosis remained significantly associated with TRS.

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Conclusions:
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