

Could we ever predict the onset of schizophrenia?



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AIM To identify the prognostic values of key changes in the prodromal phase of psychosis and consider whether these could be used to predict the onset of schizophrenia

INTRODUCTION

- Schizophrenia is a cognitive and behavioural psychiatric disorder characterised by positive symptoms, such as delusions and hallucinations, and negative symptoms, such as social withdrawal and anhedonia
- Patients usually first seek help when psychotic symptoms appear, commonly in early adulthood
- Currently, environmental risk factors for schizophrenia have been identified, as well as some genes which contribute to the disease
- However, since this disorder is characterised by symptoms rather than cause, research on the early course of psychosis could elucidate early predictive changes
- Therefore, there is need for more reliable and valid predictive factors that can be measured relatively easily in a stratified population
- Including a criteria of such prodromal symptoms in clinical management could identify individuals at higher risk of developing schizophrenia

METHODS

- A literature review was conducted assessing research on the early stages of psychosis and studies that looked at predicting the conversion to psychosis in high risk individuals
- The search mainly consisted of the PubMed database, and references from the relevant articles were also screened

1. Predicting schizophrenia using biological changes and brain imaging

- There have been some candidate predictive biomarkers identified for schizophrenia.
- Howes et al.¹ carried out PET-imaging of 24 At-Risk Mental State (ARMS) patients and found elevated striatal 18F-dopa uptake compared to controls. Hence, dopamine overactivity precedes the onset of schizophrenic prodromal individuals
- A prospective study was carried out following 30 Clinical High Risk (CHR) patients scanned using PET for at least 3 years to determine dopamine synthesis levels². Individuals who transitioned to psychosis had more synthesis of dopamine in the striatum compared to healthy subjects.
- Prodromal reductions in cortical grey matter are seen in a study involving 274 CHR patients who underwent an MRI scan at baseline, 12-month follow-up, and/or the point of conversion to psychosis³. A steeper rate of grey matter loss was seen in CHR converters to psychosis compared to CHR non-converters or healthy controls.

2. Predicting schizophrenia using symptoms in the prodromal phase

- The prodromal phase of psychosis consists of unusual behavioural symptoms and changes in thought, perception, and belief, emerging before a first episode of psychosis (FEP)
- In order to identify patients in the prodromal phase, a Criteria of Prodromal Symptoms has been developed based on attenuated positive symptoms (APS), brief limited intermittent psychotic symptoms (BLIPS), Bonn Scale for Assessment of Basic symptoms (BSABS), and combined genetic risk and functional decline. Individuals meeting this are in an ARMS or CHR state. **Table 1** below shows some of the key studies in this area

Study	Method	Outcome
Miller et al. ⁴	Tested the reliability and predictive validity of the prodromal criteria when applied to the form of a Structured Interview for Prodromal Syndromes (SIPS).	Results showed a high inter-rater reliability of 93% when diagnosing these patients.
Yung et al. ⁵	Developed the Comprehensive Assessment of At Risk Mental States (CAARMS) to prospectively diagnose pre-psychotic phenomena and followed 49 CHR patients monthly for a year or until psychosis onset.	40.8% of CHR individuals developed psychosis within 12 months and negative symptoms such as poor concentration and attention, decreased energy, altered emotional responsiveness, and poor tolerance of stress were found to be more predictive than APS.
The European Prediction of Psychosis study ⁶	Assessed 245 help-seeking prodromal patients using CHR criteria	Found a transition rate to psychosis of 19% during an 18-month follow up and a predictive value of 83.3%, showing good diagnostic accuracy

3. Predicting schizophrenia using quality of life assessments

- Impairment in domains measuring life quality such as employment status, home duties, and interpersonal relationships have been linked to schizophrenia⁷
- Low Quality of Life (QOL) and Global Assessment of Functional ability (GAF) scores were associated with a vulnerability to psychosis⁸
- Carter et al.⁹ assessed 212 high risk subjects (averaging 15 years old) on seven domains covering genetics, cognition, environment and behaviour. A 10-year follow up showed interactions of genetics with home environment and school behaviour helped forecast psychosis and schizophrenia onset

CONCLUSIONS

- Many potential methods for predicting the onset of schizophrenia using symptoms or changes observed in the prodromal phase of psychosis have been highlighted in the studies presented
- I propose for clinical management, interviews and assessments such as the CAARMS/SIPS/BSABS are used to identify those at high risk initially with only more ambiguous cases undergoing EEG or PET imaging to monitor and identify biological changes (**Figure 2**)
- By understanding the nature of the prodrome further, the number of false positives will be reduced enabling earlier monitoring and treatment of patients. Current techniques seem promising and justify the expectation that schizophrenia onset can be predicted before psychosis presents, potentially leading to preventative strategies personalised to the individual at risk.

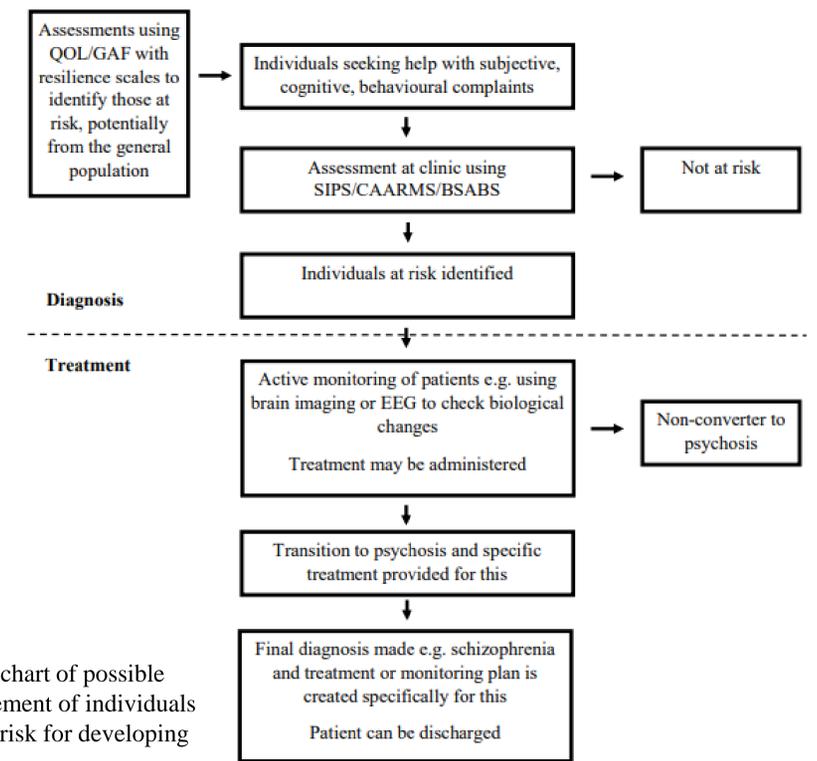


Figure 2: Flowchart of possible clinical management of individuals at clinical high risk for developing psychosis.

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