Pattern Separation Deficits in Schizophrenics Support Animal & Postmortem Work to Provide Breaking Behavioural Evidence of Impaired Neurogenesis in the Condition

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INTRODUCTION

The field became of interest to human cognitive neuroscience when Kirwan and Stark (2007) used MRI to demonstrate that DG activity increased when volunteers performed a task involving difficult object pattern separations, but not with simpler object pattern separations.

This instigated a still ongoing concerted research effort to develop compounds which may correct compromised hippocampal neurogenesis and thus treat memory disorders in a variety of clinical conditions including pathological ageing.

BACKGROUND

Recent evidence indicates that the G-protein coupled receptor, SREB2/GPR85, a known schizophrenia risk factor, negatively regulates hippocampal dentate gyrus neurogenesis-dependent spatial pattern separation in mice (Chen et al, 2012).

The demonstration by Sahay et al (2011) that increasing adult hippocampal neurogenesis is sufficient to improve pattern separation confirmed the suspected two-way relationship between DG activity and hippocampal stem cell production; thus making OPS tasks both non-invasive proofs of mechanism for compounds which target this process, as well as cognitive outcome measures.

The implications from the present study are that part of the memory deficit in schizophrenia is related to compromised DG neurogenesis, and that this deficit may respond to medications which influence hippocampal neurogenesis.


Wesnes KA  (2010). Visual object pattern separation: A paradigm for studying the role of the dentate gyrus in memory disorders. Alzheimer’s & Dementia 6:


METHODS

The CDR System OPS task was administered to 91 stable medicated schizophrenic patients aged 22 to 63 years and the results contrasted to 2,330 age-matched healthy controls.

RESULTS I: Differences to Controls

The purpose of this study was to determine if DG-sensitive OPS is selectively compromised in schizophrenia.

First data using MRI to show a pattern separation task can reflect CA3 & Dentate Gyrus Activity

HYPOTHESIS

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Results from using MRI to show a pattern separation task can reflect CA3 & Dentate Gyrus Activity.

RESULTS II: Disease Severity Comparisons

Performance on the OPS task was also assessed according to Clinical Global Impression Severity (CGI-S) scores.

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The implications from the present study are that part of the memory deficit in schizophrenia is related to compromised DG neurogenesis, and that this deficit may respond to medications which influence hippocampal neurogenesis.

This is to our knowledge the first cognitive data from an OPS task with established DG sensitivity to show a significant and large effect size-selective deficit in schizophrenics compared to normals; further supported by reliable disease severity deficits, again with large effect sizes.

REFERENCES


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