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INTRODUCTION

Compromised Neurogenesis in Schizophrenics

BACKGROUND

Recent evidence indicates that the G-protein coupled receptor, SREB2/GPR85, a known schizophrenia risk factor, negatively regulates hippocampal adult neurogenesis and thus treat memory disorders in a variety of clinical conditions including pathological aging.

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

Object pattern separation (OPS) tests could therefore reflect the quality of DG activity, and by implication provide an index of neurogenesis in man.

METHODS

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

RESULTS I: Differences to Controls

The difference in % accuracy scores between the populations in the DG sensitive measure was: 12.8 (95% CI 10.16; Effect size = 1.0) compared with -5.3 (95% CI 2.8; Effect size = 0.42) for the non-DG sensitive measure.

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RESULTS II: Disease Severity Comparisons

The effect size of the difference between CGI-S 2 and CGI-S 4 for the DG sensitive score was 1.28.

Speed scores supported the poorer accuracy scores; DG sensitive responses being 181 ms slower in CGI-S 2 than CGI-S 3, but -1 ms for the non DG sensitive score.

DISCUSSION & CONCLUSIONS

Evidence that improving neurogenesis will improve 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.

A recent review (Agius & Nandra, 2012) has identified evidence that atypical antipsychotics such as olanzapine, risperidone, paliperidone, aripiprazole and possibly quetiapine do promote neurogenesis, perhaps as a class effect, whereas first generation antipsychotics such as haloperidol or clozapine do not.

Further, the speed of the DG sensitive responses was significantly slowed (p=0.009) but not for non-DG sensitive ones (p=0.3).

No such interaction was seen in a comparable forced choice non-DG differentially sensitive verbal recognition task (p=0.57), indicating that the OPS effect was not due to response style on such tasks.

REFERENCES
