First Human Behavioural Evidence of Compromised Dentate Gyrus Neurogenesis in PD is Unrelated to Poor Attention and Impulsivity

Keith A. Wesnes1,2; David S. Miller3; David J. Burn4
1Bracket, Goring-on-Thames, UK; 2Centre for Human Psychopharmacology, Swinburne University, Melbourne, Australia; 3Bracket, Wayne, PA, USA; 4Institute for Ageing and Health, Campus for Ageing and Vitality, Newcastle University, Newcastle, UK

BACKGROUND

- Destruction of dopaminergic neurones decreases Dentate Gyrus (DG) neurogenesis in rodents and primates.
- Post-mortem work in Parkinson's disease (PD) patients has identified evidence suggesting compromised hippocampal neurogenesis.
- In both animals and man, difficult discriminations in object pattern separation (OPS) tasks reflect DG activity and thus potentially neurogenesis.
- The object of this study was to provide the first human behavioural evidence that DG neurogenesis is compromised in PD.

METHODS

Population
- 348 PD Patients
- 1578 healthy age matched controls

All tested on a range of automated tests of cognitive function from the CDR System

Domains assessed included attention, information processing and the CDR System Object Pattern Separation Task

The populations were compared using ANCOVA, with age fitted as a covariate

RESULTS

- The PD patients were significantly poorer than controls on the ability to correctly reject the closely similar pictures:
  - F(1,1751) = 72, p<0.0000001
- The PD patients were not poorer than controls on the ability to correctly identify the original pictures:
  - F(1,1751) = 1.3, p=0.25
- Speed also slowed to slightly greater extent, indicating poor accuracy in PD on closely similar pictures due to rushed responding

- The PD patients were also impaired on various measures of attention, information processing & impulsivity:

  - Could the selective Object Pattern Separation (OPS) impairments be influenced by impairments in these other important cognitive domains?
  - To examine this possibility, ANCOVA was conducted on the differences in correct detections between the controls and PD groups.
  - The ANCOVA was then repeated fitting each other measure as a covariate

DISCUSSION & CONCLUSIONS

Evidence that improving neurogenesis will improve performance on object pattern separation tasks

- The PD patients showed a selective deficit on a dentate gyrus sensitive measure in an object pattern separation (OPS) task
- This deficit was independent of notable impairments in the PD patients in: the ability to focus and sustain attention; the ability to efficiently process information and to withhold inappropriate responses
- This is to our knowledge the first behavioural demonstration of compromised OPS in PD