Parkinson’s patients have compromised performance on an object pattern separation task suggesting decreased neurogenesis in the dentate gyrus

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THE DENTATE GYRUS

- The seminal discovery that the human dentate gyrus (DG) retains its ability to generate neurons throughout life (Erickson et al., 1998), has raised the possibility that therapies could be developed to protect or promote this neurogenesis as it deteriorates due to ageing, insult and disease.

- Destruction of dopaminergic neurones decreases neurogenesis in the Dentate Gyrus (DG) of rodents and primates.

- O’Sullivan et al (2011) identified in post-mortem analysis that Parkinson’s disease (PD) patients had evidence of reduced neurogenesis in the DG which was related to the duration of illness.

- This suggests that neurogenesis could be compromised in Parkinson’s disease (PD).

THE CDR SYSTEM PICTURE RECOGNITION TASK: AN OBJECT PATTERN SEPARATION TASK

- The task measures delayed object recognition memory.

- The subject initially sees 20 different pictures of everyday scenes and objects, presented one at a time on a computer screen.

- Subsequently after an interval of around 10 minutes, these pictures are re-presented, intermixed with 20 very similar but different pictures (see examples below).

- For each picture, the volunteer has to decide whether or not the picture was shown originally by pressing either YES or NO buttons as quickly as possible. (Ohm, 2007; Tatebayashi, 2003).

Part A: 20 pictures are presented to the subject at the rate of 1 every 3 seconds.

Part B: 15 minutes later, the 20 pictures are re-presented, mixed with 20 very similar ones.

For each picture, the subject is required to press YES as quickly as possible if it was the original picture, or NO if it is a similar but different picture.

RESULTS

- PD patients show a medium to large effect size for PD patients for an increase in the DG compared to controls (PD 86.7%, Controls 87%, p<0.0001), whereas they were poorer at rejecting the similar pictures (PD 67.3%, Controls 76.7%, p< 0.0001).

- The effect size was 0.73, a medium to large effect size, indicating its clinical relevance.

- PD patients were not different to controls on the ability to recognise the original pictures (PD 86.7%, Controls 87%, p<0.0001), whereas they were poorer at rejecting the similar pictures (PD 67.3%, Controls 76.7%, p<0.0001).

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- However, the deficit to attention and information processing as assessed by the Power of Attention measure was impaired with respect to controls with an effect size of 2.7 (See Graph 2).

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- This effect is independent of the much larger information processing deficit in the condition, and suggests these deficits are underpinned by different neuroanatomical and/or neurochemical deficits.

- To our knowledge this is the first demonstration of compromised object pattern separation in PD, suggesting that neurogenesis in the DG is decreased in PD, mainly due to dopaminergic loss.

- Of further importance are the neuroprotective effects of compounds in development for PD, for example rasagiline, which was found to promote neurogenesis in rats (Silash et al., 2006).

- This task could therefore serve as a proof of principle that such compounds were influencing neurogenesis in the DG.

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REFERENCES

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Conclusions

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