Evidence that Compromised Neurogenesis in Alzheimer’s Disease is Linked to APOE ε4 Status and CSF Aβ42
Keith A. Wesnes
Bracket, Goring-on-Thames, UK and Centre for Human Psychopharmacology, Swinburne University, Melbourne, Australia

BACKGROUND & OBJECTIVES

Evidence that Compromised Neurogenesis in Alzheimer's Disease
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RESULTS

AD related impairments in various domains & measures As would be expected the AD patients showed large effect sized impairments in all CDR System domain separations. AD patients also showed significantly impaired pattern separation tasks. This finding is consistent with preclinical work and suggests that therapies designed to reduce brain power of attention may promote neurogenesis and associated improvements in pattern separation. This study employed a OPS validated task and this analysis identified:

1. Significant effects of APOE ε4 on pattern separation in AD patients
2. Significant effects of APOE ε4 on pattern separation in healthy older controls
3. Significant effects of APOE ε4 on pattern separation in young controls
4. Significant effects of APOE ε4 on pattern separation in healthy younger adults

DISCUSSION & CONCLUSIONS

In man neurogenesis occurs in two major brain areas, one being the hippocampal dentate gyrus (DG), which is also a region heavily involved in pattern separation.

DG activity can be monitored in man by measuring the ability to make difficult discriminations in object pattern separation (OPS) tasks.

Preclinical work has associated APOE ε4 status & declining levels of Aβ42 with reduced dentate gyrus (DG) activity & disrupted neurogenesis.

This study employed a OPS validated task and this analysis identified:

1. CSF Aβ42 levels to be related to difficult OPS in AD patients
2. ε4 homologues to show a selective decline on the ability to make difficult OPS
3. This finding is consistent with preclinical work and suggests that therapies designed to reduce brain levels of beta amyloid may promote neurogenesis
4. This task which takes less than 4 minutes can thus serve as a proof of principle as well as being an outcome measure for such therapies