

THE APPLICATION OF COGNITIVE NEUROSCIENCE TO CLINICAL RESEARCH III: EVALUATING TREATMENTS TARGETING HUMAN HIPPOCAMPAL NEUROGENESIS

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Background & Objectives: The seminal discovery that the human dentate gyrus (DG) retains its ability to generate neurons throughout life has raised the possibility of developing therapies to protect or promote such neurogenesis as it deteriorates due to ageing, insult and disease. Pattern separation has been demonstrated to be under the control of the DG, and fMRI studies have identified the DG to be highly and selectively active when humans perform difficult visual object pattern separation tasks. The CDR System picture recognition task assesses visual object pattern separation, and has provided evidence of compromised neurogenesis with ageing in over 3000 healthy individuals as well as patients with Mild Cognitive Impairment. The present investigation examined various clinical conditions for evidence from this task of compromised DG activity, and thus potentially compromised neurogenesis.

Methods: Various clinical populations who had performed the CDR System picture recognition task were examined for evidence of selectively compromised ability to make difficult discriminations. The conditions evaluated were late life depression, Huntington's disease, chronic pain, Parkinson's disease, oncology, schizophrenia, stroke, epilepsy, Alzheimer's disease, vascular dementia and dementia with Lewy Bodies

Results & Discussion: Evidence of impaired neurogenesis was identified in many but not all of the clinical populations. Where it was identified, it was often consistent with pre-clinical data showing impaired DG neurogenesis. The task could therefore be a useful tool to evaluate the efficacy of novel compounds intended to promote, maintain or restore neurogenesis. Importantly the task could additionally serve as a non-invasive biomarker for compounds which may influence the DG.