Does chronic stress alter reelin in the entorhinal cortex?

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INTRODUCTION

Alzheimer's Disease (AD):
- Most common form of dementia, due to amyloid-β plaques and hyper-phosphorylated tau[1].

Chronic stress (CS):
- History of CS shown to increase risk of both depression and AD [2,3]

Reelin:
- Protein with roles in neuronal migration[4], synaptic growth, reducing amyloid-B toxicity, and inhibiting phosphorylation of tau[5].
- Dysregulated in neuropsychiatric disorders such as AD[5] and depression.
- Injection with reelin restores CS induced reelin dysregulation..

Entorhinal cortex (EC):
- Crucial for episodic and spatial memory, first region showing changes in AD[1].

METHODS

A. Rats (n=36) were exposed to a cyclic corticosterone (CORT) model[6], alternating 3 weeks CORT injections (20mg/kg) or saline with 3 weeks of rest.
   - Last day injected with 3µg of reelin or saline.
   - Quantified depression-like behaviour using the forced swim test (FST).
   - Evaluated spatial memory using the Object in Place Test (OBiPT)

B. Collected tissue and used immunohistochemistry to stain reelin⁺ cells.

C. Evaluated reelin positive (⁺) cell density across equal volumes per subject.

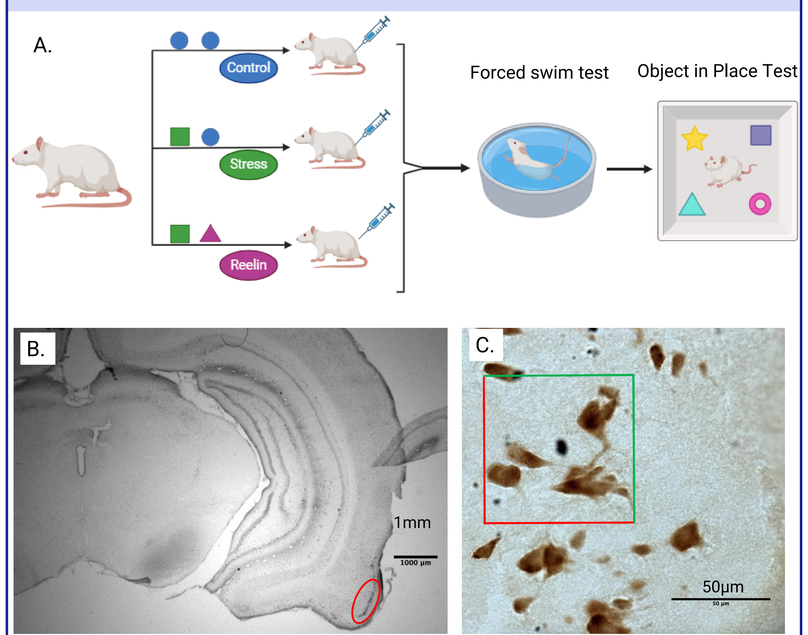

Figure 1. Overview of experimental procedures. A. cyclic CORT model followed by behavioral testing. B. Location of the EC. C. Reelin ⁺ cells (brown) surrounded by box with inclusion/exclusion regions marked.

RESEARCH QUESTIONS

1. Will CS alter the density of reelin⁺ cells in the EC?
2. Will treatment with reelin restore levels of reelin⁺ cells in the EC, following CS?
3. Will alterations in the density of reelin⁺ cells relate to the depressive symptoms observed?
4. Will alterations in the density of reelin relate to the change in spatial memory seen?

NO RELATION BETWEEN FST IMMOBILITY AND REELIN

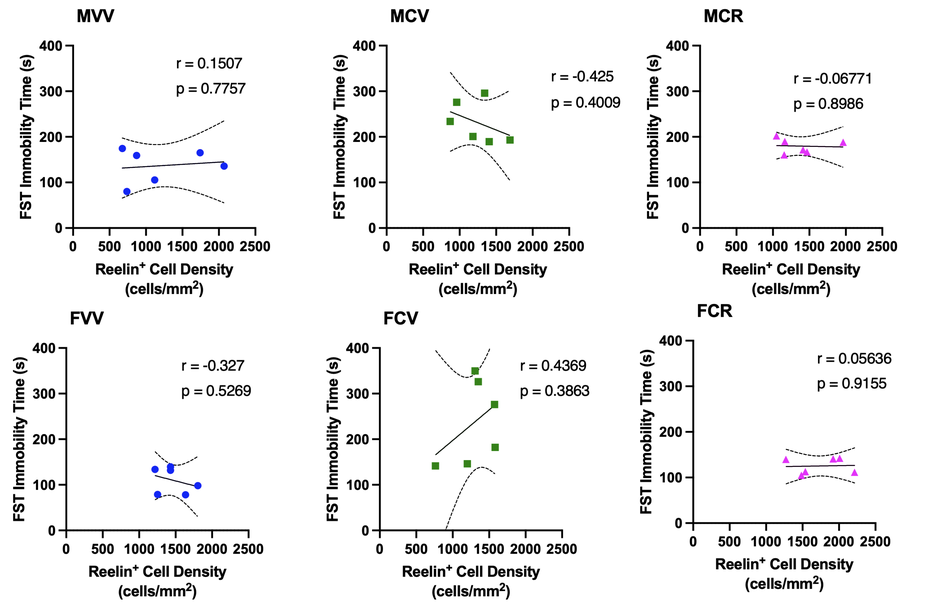

Figure 2. Correlations between reelin⁺ cell density and FST immobility time.

REELIN⁺ CELL DENSITY CORRELATES WITH SPATIAL MEMORY IN MALES

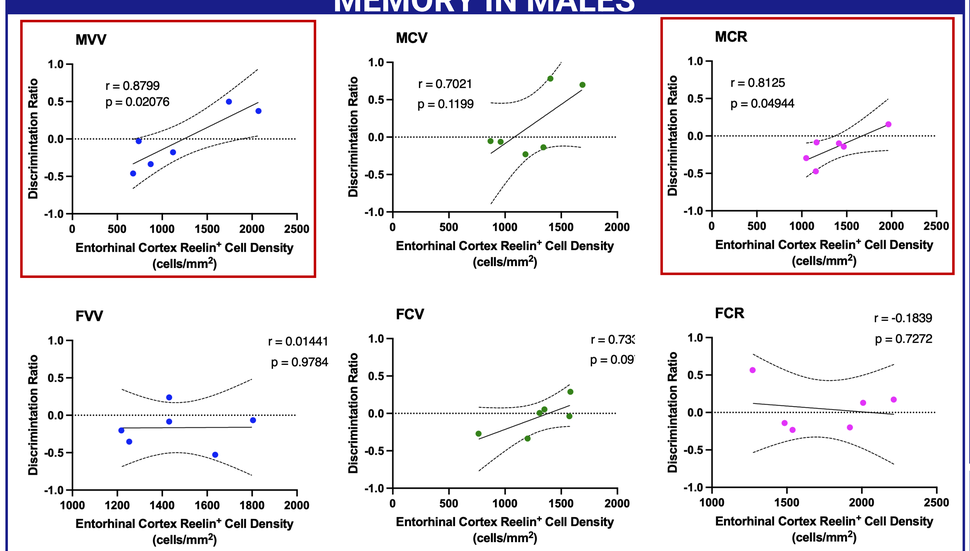

Figure 3. Correlations of discrimination ratio in OBiPT and EC reelin⁺ cell density. There is a positive correlation in MVV, that is disrupted by CORT and rescued by a single reelin injection. There is no correlation observed in females.

NO CHANGE IN REELIN⁺ CELL DENSITY

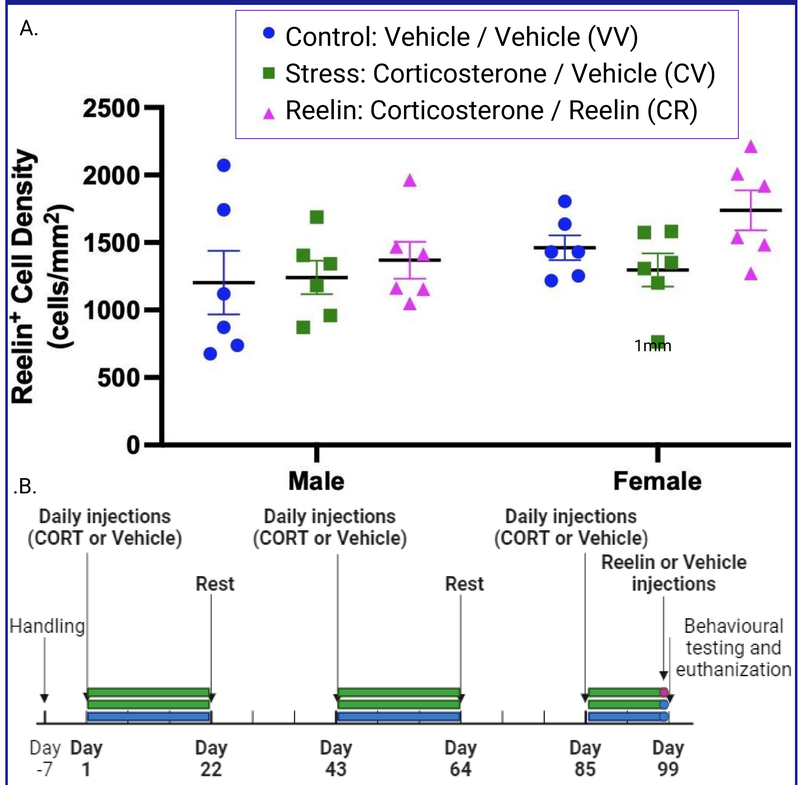

Figure 4. A. Reelin⁺ cell density across all groups. Two way ANOVA revealed no significant differences in sex, condition, or interaction of main effects (all p > 0.19). Mean, error bars: SEM. B. Experimental timeline

DISCUSSION

Results show:
- No changes in reelin⁺ cell density following CS, or reelin injections
- No correlation between depression-like behaviour and reelin⁺ cell density.
- Correlation between male rat EC reelin⁺ cell density and spatial memory is disrupted in CS, but recovered with a reelin injection. Sex specific, this was only seen in males

Therefore:
- CS does not affect reelin in the EC as it does other brain regions.
- CS is not solely responsible for disruption of reelin in the EC.
- Reelin disruption may be involved in reduction of spatial memory following CS.
- The sex specific differences in correlations warrant additional studies to evaluate how these difference may relate to epidemiological or clinical sex differences in AD and depression.

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