Introduction

- Early life stress (ELS) is highly associated with development of psychopathology and mood disorders in adulthood [1].
- Environmental factors can interact with genes, e.g. environment can lead to significant risk gene expression changes or a genetic factor can influence sensitivity to a particular environment.
- Genetic studies have identified variation in the gene calcium voltage-gated channel subunit alpha 1C (CACNA1C) to increase risk for several psychiatric disorders [2].
- CACNA1C encodes an alpha-1 subunit of voltage-gated calcium channels (VTCCs), which mediate calcium influx into cells.
- In humans, SNPs in CACNA1C has been shown to interact with adult trauma to predict depression [3].
- In rodents, acute and chronic stress in rats causes an increase in VTCCs in the hippocampus, cortex and basolateral amygdala and Cacna1c+/- mice have increased susceptibility to chronic social defeat stress [4].
- Aim: To investigate the expression of Cacna1c following prepubertal stress (PPS).

Methods

- PPS was conducted on rats from PND25-27 and mRNA analysed by qPCR and iSH. Protein analysis was done by Western Blot.
- Cacna1c+/- rats and PPS rats where subject to trace fear conditioning. Rats were conditioned with 0.5mA footshock. Bursts of 75-86db white noise formed the CS, and CS-US were separated by an interval. All animals were presented with 10 CS-US pairings. Recalls took place 24 and 48 hours later.

PPS and Cacna1c heterozygosity both result in trace auditory fear conditioning impairments

In trace conditioning, there is a 30 sec gap between white noise offset (CS) and the footshock (US); learning the trace association is both hippocampal and neurogenesis dependent.

Conclusions

- Male rats who has been subject to PPS have decreased Cacna1c mRNA in the hippocampus, specifically the CA1 and CA3. Female rats have intact Cacna1c expression.
- Male rats also tend to a decreased Cav1.2 protein level within the hippocampus.
- Human males who had suffered ELS also show a decreased Cacna1c mRNA.
- Both PPS and Cacna1c+/- rats show deficits in trace auditory fear conditioning, however PPS rats show decreased fear responses whereas Cacna1c+/- rats show increased fear responses. This suggests that impairments in stress pathways and Cacna1c affects hippocampal-dependent tasks.

References