07 - Strong acute-stress impairs cortical synaptic plasticity in the amygdala

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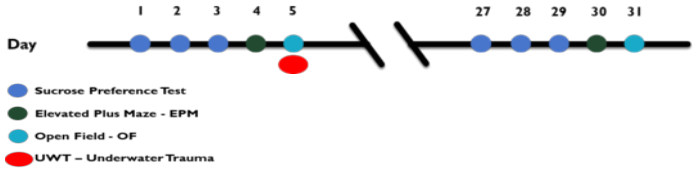
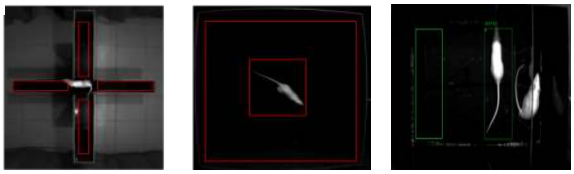
Introduction

Learning is a key process that allows individuals to adapt to the environment. Considerable evidence indicates that new memories are formed upon a large network of pre-existing knowledge. This implies that learning is highly influenced by previous experience and that previous consolidated memories can be reactivated during new learning. This is particularly relevant in the context of traumatic memories, in which the formation of a particular association leads to a disruptive behaviour. In post-traumatic stress disorder (PTSD) an over-generalization and hyper-reactivity of fear responses is observed after exposure to a traumatic event. There is clear evidence that subjects with PTSD show not only a behavioural sensitization to stress and an over-generalization to neutral stimuli but also an impaired extinction of the initial association established during the traumatic event. This suggests that PTSD may alter the normal dynamic flow of memory. The link between endocannabinoid signalling, the acquisition of fear memories and stress is well established. We have recent data suggesting that CB1R activation restricts synaptic cooperation and competition in the amygdala by reducing thalamic synaptic activation. Also, we have preliminary evidence that CB1R are differently expressed between thalamic and cortical presynaptic boutons. These observations, together with a recent report that endocannabinoid synthesis is sensitized by previous negative events, support the hypothesis that endocannabinoid system function as a "gatekeeper" restricting fear-memory acquisition. We aim to 1) using an animal model of PTSD, assess the properties of synaptic plasticity in the thalamic and cortical afferents to the lateral amygdala; 2) assess whether modulation of the cannabinoid signalling regulates the development of a PTSD phenotype.

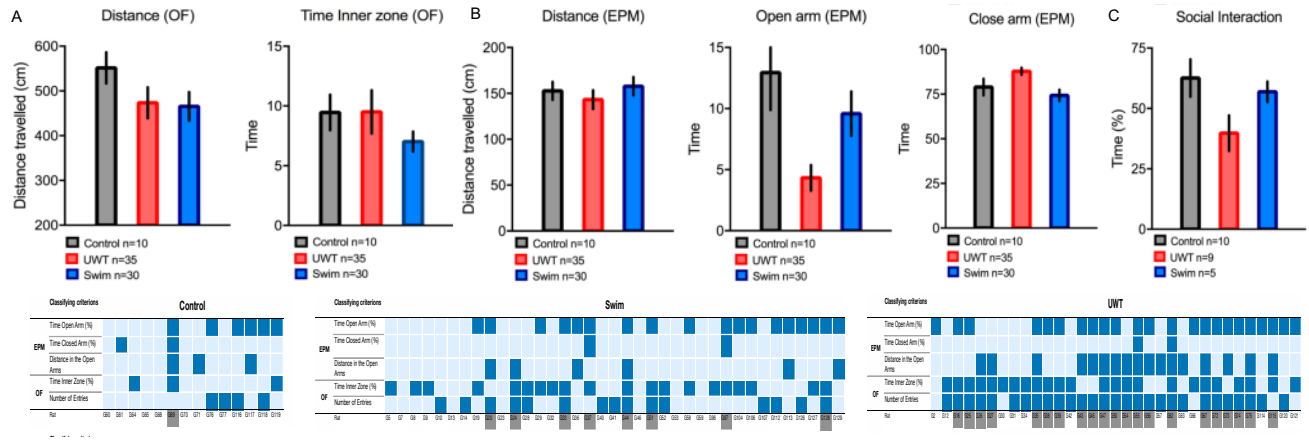
Results

We use a combination of behavioural analysis and electrophysiology to assess the behavioural profile of the animals and synaptic properties in the amygdala. We analysed the individual scores of the animals in two time points (Figure 1) and defined a behavioural profile according to the deviation to the control group.

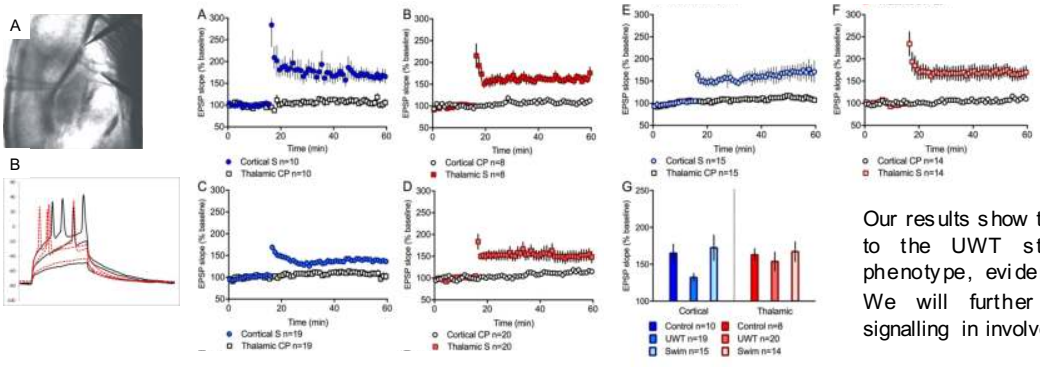




We observed that exposing animals to a single high-stressor (UWT) lead to the development of an anxiety profile that is expressed in a lower exploration of the open arm of the elevated plus maze (EPM - B) as well as a lower time spent in the inner-zone of the open field arena (OF – A; Figure 2). No change was observed in the sucrose-preference test suggesting that a depressed-like phenotype is not present. In a selected group of animals we performed an additional behaviour test, the social-preference test an observed an impairment in stressed exposed animals (C).



Patch –clamp recordings of amygdala pyramidal cells (LA) showed that cells from stressed animals are more excitable (lower action-potential threshold) although their resting membrane potential is unchanged (Figure 3, A/B). WE also observed that cortical LTP in unpaired in stressed exposed animals (Figure 4 – C/D), as compared with Swim (E/F) and control animals (A/B).



Our results show that not all animals exposed to the UWT stressor develop a PTSD phenotype, evident in the individual profile. We will further address whether CB1R signalling in involved in resilience.

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