Title: Fear not to remember: impact of acute stress in amygdala synaptic cooperation

Context

Learning is a key process allowing individuals to adapt to the constant challenges of the environment. It is now well accepted that learning involves the storage of information in the form of long-lasting memories. However, the acquisition of maladaptive memories has a profound impact in the way we govern our lives and interact socially with others. Acquisition of memories requires a process of consolidation, in which unstable memories, prone to be lost, become stabilized as long-lasting memories. This information is not, however, stored as an immutable trace. Remembering turns previous memories in an active and unstable state. This dynamic aspect of memory raises several interesting and still open questions. Are all reactivated memories updated? Can one determine the rules underlying memory updating? These questions are 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, such as sexual assault, warfare, traffic collisions, terrorism or other threats on a person’s life. Individuals with PTSD show a behavioural sensitization to stress, an over-generalization to neutral stimuli and also intrusive recollections of the initial association established during the traumatic event. This suggests that PTSD alters the normal dynamic flow of memory. If one can identify how traumatic events alter the dynamics of memory formation, then it is possible to modify traumatic memories and decrease the burden caused by PTSD.

Experimental Approach

Here, we explore an integrative approach to address the dynamics of memory, combining cellular physiology with behavioural approaches in the context of PTSD. We propose that traumatic events alter the dynamics of synaptic plasticity in amygdala synapses. We have recently found that synapses receiving inputs from thalamic and cortical projections, a circuitry know to be key in fear responses, can cooperate re-enforcing each other. The temporal window in which thalamic and cortical synapses cooperate is determined by the endocannabinoid signalling. Using a model of PTSD combined with an individual profiling of animal behaviour, we aim to test whether the development of PTSD leads to a change in thalamic and cortical synaptic cooperation. Moreover, since endocannabinoid signalling is modulated by stress, we aim to test whether modulation of this system reverts PTSD induced synaptic modifications. Understanding brain function in normal and pathological conditions is a major issue in our modern societies. Although the scientific community has now an increasing body of knowledge on the cellular and molecular mechanisms of memory formation, we fail to understand the dynamic evolution of memories. It is clear that our behaviour is by large determined by our previous experience. Uncovering how memories are formed, maintained and updated will allow us to decrease the impact of maladaptive memory formation. To achieve this ambitious goal, one needs an integrative approach. This proposal presents an opportunity to obtain such an integrative view while opening the possibility to a new therapeutic tool to minimise the impact of PTSD.