

Impact of life history on fear memory and extinction in mice

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Cumulative stress throughout life time is one of the predominant environmental risk factors for several psychiatric disorders, such as depression or anxiety disorders. So far different hypotheses exist that address the correlation between early and adult chronic stress and the individuals' vulnerability to psychiatric diseases. The match/mismatch hypothesis of psychiatric disease states that the early life environment shapes coping strategies in a manner that enables individuals to optimally face similar environments later in life (Santarelli et al. 2014).

In the present study we aim to determine the influence of a matched/mismatched life history on fear memory and extinction in mice. Therefore, five groups of C57Bl/6J male mice underwent differential treatment (AA = adverse early + adverse late environment, BB = beneficial early + beneficial late environment, AB = adverse early + beneficial late environment; BA = beneficial early + adverse late environment, C = Control) from prenatal stage till the age of 75±2 days before being tested for fear memory and extinction processes in a Pavlovian fear conditioning paradigm.

To determine whether life history modulates neurophysiological activities in brain regions related to fear and anxiety, we recorded from the infralimbic region of the medial prefrontal cortex (IL, mPFC) and the lateral amygdala (LA), respectively. Fear memory and extinction of conditioned fear was observed in parallel to recordings of neuronal activity during phases of retrieval (R1), extinction learning (R2-R6), recall of fear extinction (E1-E2) and spontaneous recovery of fear (SR).

First results indicate an impairment of fear extinction in animals raised in an AA and BA environment which is accompanied by theta coupling of IL and LA during R1, R6 and E1. In contrast, animals with a beneficial early and late background in their life history showed a trend towards enhanced extinction learning. Interestingly, animals initially raised adversely and afterwards encountering a beneficial environment display similar behaviour when compared to control animals.

These preliminary data suggest that environmental factors influence fear related behaviours, contributing to a differential outcome in fear memory and extinction depending on the individual life history in mice.

- Santarelli S, Lesuis SL, Wang XD, Wagner KV, Hartmann J, Labermaier C, Scharf SH, Müller MB, Holsboer F, Schmidt MV. Evidence supporting the match/mismatch hypothesis of psychiatric disorders. *Eur Neuropsychopharmacol.* 2014 Jun; 24(6):907-18.