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Abstract of the dissertation

Theme of the dissertation– Refinement of neuronal networks in rodent prefrontal cortex and hippocampus: Critical impact of early and late social experiences

ABSTRACT

The process of weaning programmes the physiological and neurobehavioural development of various animal species and is thus a critical formative period for adult behaviour. The neural substrates which may underlie these behavioural changes are largely unknown. This study for the first time show that the timing as well as the amount of social contact with family members significantly interferes with the refinement of prefrontal cortical and hippocampal synaptic networks.

Studies have quite intensively investigated the critical importance of emotional experience (for instance, time of weaning) at behavioural level. In addition, studies have provided compelling evidence that during development environmental factors (such as social or isolated environment) dynamically modify animal's behaviour and brain development. Nevertheless, the impact of these two different developmental time windows of emotional experience have never been systematically studied and the neural mechanism remains unknown. In this study, I tested our working hypothesis that during late childhood the neuronal networks in various limbic areas such as the prefrontal cortex and hippocampus are reorganized in response to the timing and the extent of social interaction with the mother and the siblings. This was done by investigating the impact of time point of weaning (21 vs. 30), of social environments (social vs. isolation) and in addition, by investigating the *interactions* between these two factors on the neuronal morphology in the prefrontal cortex and hippocampus. The prefrontal cortex and the hippocampus are part of the limbic system which are involved in emotional self-regulation and the expression of emotional behaviours. Since, the time of weaning appears to be a major emotional challenge during late childhood it can be assumed that this transition to independency should involve major structural changes in limbic areas such as the prefrontal cortex and hippocampus, which are involved in emotional behaviours.

The findings of this study demonstrate that emotional experience (i.e. the extent of social experience with mother and the siblings) induces dendritic and synaptic reorganization, which occurs in a highly temporal, regional and dendrite-specific manner. The development of spine density was particularly sensitive to the amount of preweaning social experience, as the animals that spent less time with their mother i.e. early weaned demonstrated elevated spine densities in their dendrites of anterior cingulate cortex (ACd) and hippocampus. The dendritic length and complexity of apical dendrites in the prefrontal area, anterior cingulate cortex (ACd) and orbitofrontal cortex (OFC) and in the CA3 area of hippocampus displayed only the *interactions* between the factors time of weaning x postweaning social environment and not the effect of time of weaning and social conditions alone. In the anterior cingulate cortex and in CA3 area, the most socially deprived group (early weaning and isolated postweaning i.e. EWI) displayed longer and more complex apical dendrites compared to other animals. In contrary, in orbitofrontal cortex these animals displayed reduction in apical dendritic length and complexity. In all these regions, the length and the complexity of basal dendrites remained unaffected by either treatment. In dentate gyrus, the dendritic length and complexity of granular neurons, mainly in the infra pyramidal layer of dentate gyrus displayed not only *interactions* between time of weaning x postweaning social environment but also the influence of time of weaning per se, and of social conditions alone. Similar to that in ACd and CA3, in dentate gyrus the animals with fewest social experience or EWI demonstrated longer and more complex infra and supra granular dendrites compared to other animals. Taken together, the findings demonstrate that the timing as well as the amount of social contact with family members significantly affects the refinement of prefrontal cortical and hippocampal synaptic networks which as an integral part of the limbic system are essential for emotional and cognitive behaviour.

In summary, the findings of this study may provide the neurobiological substrate for the behavioural changes induced by different emotional experiences.