Ruprecht-Karls-Universität Heidelberg

Medizinische Fakultät Mannheim

Dissertations-Kurzfassung

The hippocampus in contextual fear conditioning: Structural, functional and genetic aspects and their implications for psychopathology

Autor: Sebastian Pohlack
Institut / Klinik: Zentralinstitut für Seelische Gesundheit Mannheim (ZI)
Doktormutter: Prof. Dr. H. Flor

The present thesis focuses on the role of the hippocampus during differential contextual fear conditioning in healthy humans. Therefore, structural and functional aspects of the hippocampus are investigated using imaging methods.

Based on animal as well as human research implicating the hippocampus and amygdala in contextual fear conditioning, the first study investigated the impact of structural properties of those two regions on associative learning in 58 healthy volunteers using a differential fear conditioning paradigm with contextual stimuli. To evaluate conditioning, skin conductance responses as well as ratings of emotional valence, arousal and contingency were assessed in two groups of participants (each N = 29) with relatively large versus small hippocampal volumes. The results suggest that persons with larger but not those with smaller hippocampal volumes learned to successfully differentiate between the aversive and safe context as indicated by skin conductance responses. Reanalysis of the skin conductance response data using subvolumes of the hippocampus as explanatory variable showed that especially the volume of the right hippocampus was related to differential learning. Further analysis revealed that posterior but not anterior hippocampal subvolumes had a significant relationship with verbal self-reports which is in line the assumed role of that part in cognitive processes such as memory formation. In contrast, amygdalar volumes had no significant association with any of the employed measures. While neither total hippocampal nor amygdalar volumes were associated with verbal self-reports, total brain volume was - suggesting cortical structures to be involved in these more cognitive evaluation processes. In sum, the study showed the importance of the hippocampus for differential contextual fear conditioning in humans and may have implications for anxiety disorders.

In the second study the role of contextual fear conditioning for schizophrenia as a disorder beyond the anxiety spectrum, where contextual processing and hippocampal functioning impairments have been reported, was investigated. Further, the impact of the schizophrenia vulnerability gene neurogranin, which is abundantly expressed in the hippocampus, on aversive contextual learning, was assessed. Using healthy volunteers (N = 112) confounding variables typically present in patients such as medication could be excluded. Again, conditioning performance was assessed using skin conductance responses and verbal self-reports. Further, neuropsychological variables and hippocampal volumes were determined. Both allele groups learned to successfully differentiate the two conditioning contexts as indicated by skin conductance responses and ratings of emotional valence, arousal and contingency. Additionally, carriers of the neurogranin risk allele did not significantly differ in their hippocampal volumes from carriers of the resilience allele. In contrast, risk allele carriers showed significantly reduced activation in the left hippocampus during acquisition of contextual fear conditioning. Given that schizophrenia is a complex disorder with many factors contributing to the development of the disorder, the observed decreased hippocampal activation during the learning phase might represent a vulnerability factor for schizophrenia. This corroborates previous findings from conditioning studies using aversive associative learning paradigms where 30-50% of schizophrenic patients showing no learning at all as well as neuroimaging studies reporting decreased hippocampal activity during memory tasks in schizophrenics.