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Influence of emotional deprivation on the neurochemical and structural development of limbic structures and behavior in rodents (*Octodon degus*).

Fatherless children are at dramatically greater risk of developmental maladaptation, drug and alcohol abuse, poor educational performance and criminality. The aim of this study was to test our working hypothesis that the absence of paternal care interferes with the neuronal development of prefrontal and limbic areas, which most likely results in behavioral changes. Animal models for paternal deprivation represent a unique model to analyze psychopathological disorders and deficits in the development of personality or of intellectual and social capabilities associated with the loss of paternal care

I identified the behavioral consequences and the neuronal substrate, which underly such an abnormal development. In the biparental animal model *Octodon degus* the influence of paternal care on social, anxiety, learning and impulsive behavior and the establishment of synaptic wiring and neurochemical characteristics were analyzed in cortical and subcortical brain regions. The quantitative comparison of biparental and single-mother families revealed that single-mothers do not compensate the lack of paternal care, i.e. the pups which are raised in single-mother families experience significantly less parental care and consequently are raised under partly socio-emotional deprivation. Paternally deprived, juvenile animals showed decreased durations of pup-parent allogrooming and increased frequencies of play-fighting episodes. Furthermore, adult fatherless animals displayed components of impulsive behavior, impaired learning performance and higher levels of anxiety. On the neuro-morphological/neurochemical level fatherless pups displayed a reduced number and density of dendritic spines, which represent excitatory synapses, on layer II/III pyramidal neurons in the orbitofrontal cortex (juvenile and adult) and lateral amygdala (juvenile). In addition, apical dendrites in the orbitofrontal cortex were significantly shorter in father-deprived adult animals, whereas neither changes of dendritic lengths were observed in the juvenile orbitofrontal cortex or on amygdalar pyramidal neurons (juvenile and adult), nor deprivation-related changes in neuronal morphology in the hippocampal formation. Concerning the inhibitory GABAergic system neurochemically characterized by their expression of the calcium-binding proteins Parvalbumin and Calbindin-D28k) and CRF-containing cells differences in all analyzed regions were prominent in the father-deprived animals compared to biparentally raised animals: juvenile and adult fatherless animals showed an increased density of Parvalbumin-expressing and CRF-containing neurons in the orbitofrontal cortex as well as in the basolateral amygdaloid complex. In the primary output region of the amygdala, the central nucleus, also an increased density of Parvalbumin-expressing interneurons was found. In contrast to observations in the laboratory rat virtually no CRF-immunostained neurons, but heavily immunoreactive, dense clusters of CRF-positive fibers were found in the central nucleus, whose density reamained unchanged in the fatherless animals. The hippocampal formation of fatherless animals showed an enhanced density of Parvalbumin-expressing interneurons in the dentate molecular layer and in the pyramidal cell layer of the CA1 region (juvenile animals), whereas in adult fatherless animals a reduced density was observable in the pyramidal cell layer and the CA1 region compared to biparentally raised animals. Furthermore, father-deprived animals showed a decreased cell density of Calbindin-D28k-expressing GABAergic neurons in the basolateral amygdaloid complex and the central nucleus, whereas an increased density of this interneuron subpopulation was seen in the hippocampal granule cell layer. No changes were observed of Calbindin-D28k-expressing GABAergic neurons in the orbitofrontal cortex of fatherless animals. A reduced density of CRF-containing cells in the dentate gyrus (adult animals), in the pyramidal an oriens cell layer of father-deprived animals was observed. In addition, the density of Tyrosinehydroxylase(TH)-containing fibers was altered in fatherless animals: father-deprived animals dsplayed an increased density of TH-positive fibers in the lateral orbitofrontal cortex, the central nucleus of the amygdala (juvenile animals) and in the hippocampal formation, whereas no changes of TH fiber density was obvious in the basolateral amygdaloid complex.

I interpret those findings as indication of an alterd function of cortical and subcortical limbic brain structures in the fatherless animals, which correlate with the observed changes in impulsivity, learning and anxiety-related behavior of father-deprived animals.