

Increased anxiety and decreased sociability induced by paternal deprivation involve the PVN-PrL OTergic pathway

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Abstract Early adverse experiences often have devastating consequences. However, whether preweaning paternal deprivation (PD) affects emotional and social behaviors and their underlying neural mechanisms remain unexplored. Using monogamous mandarin voles, we found that PD increased anxiety-like behavior and attenuated social preference in adulthood. PD also decreased the number of oxytocin (OT)-positive neurons projecting from the paraventricular nucleus (PVN) and reduced the levels of the medial prefrontal cortex OT receptor protein in females and of the OT receptor and V1a receptor proteins in males. Intra-prelimbic cortical OT injections reversed the PD-induced changes in anxiety-like behavior and social preferences. Optogenetic activation of the prelimbic cortex OT terminals from PVN OT neurons reversed the PD-induced changes in emotion and social preference behaviors, whereas optogenetic inhibition was anxiogenic and impaired social preference in naïve voles. These findings demonstrate that PD increases anxiety-like behavior and attenuates social preferences through the involvement of PVN OT neuron projections to the prelimbic cortex.

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Introduction

Social attachments can facilitate reproduction, increase survival, provide a sense of security and reduce feelings of stress and anxiety in many species (Coria-Avila et al., 2014). In humans, attachment is especially important during early development because disruption of filial attachment in children (e.g., abuse, neglect or the death of a parent) increases their vulnerability to emotional disorders at a later age (Agid et al., 1999; Reinkens et al., 1999).

By the end of 2013, it was estimated that over 61 million children in rural hometowns were missing one or both parents (more often the father) throughout China (All-China Women's Federation, 2013). Neonatal social or paternal deprivation (PD) has been proven to exert a profound and persistent influence on the physiological and behavioral development of offspring. Neonatal rodents physiologically and emotionally depend on their parents. For example, PD impairs sociability (Bambico et al., 2015; Jia et al., 2009) and social recognition (Cao et al., 2014), reduces parental

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