Early Social Enrichment Shapes Social Behavior and Nerve Growth Factor and Brain-Derived Neurotrophic Factor Levels in the Adult Mouse Brain

Igor Branchi, Ivana D’Andrea, Marco Fiore, Veronica Di Fausto, Luigi Aloe, and Enrico Alleva

Background: Early experiences produce persistent changes in brain and behavioral function. We investigate whether being reared in a communal nest (CN), a form of early social enrichment that characterizes the natural ecological niche of many rodent species including the mouse, has effects on adult social/aggressive behavior and nerve growth factor (NGF) and brain-derived neurotrophic factor (BDNF) levels in mice.

Methods: The CN consisted of a single nest where three mothers kept their pups together and shared care-giving behavior from birth to weaning (postnatal day 25).

Results: Compared to standard laboratory conditions, in CN condition, mouse mothers displayed higher levels of maternal care. At adulthood, CN mice displayed higher propensity to interact socially and achieved more promptly the behavioral profile of either dominant or subordinate male. Furthermore, CN adult mice showed higher NGF levels, which were further affected by social status, and higher BDNF levels in the brain.

Conclusions: Our findings indicate that CN, a highly stimulating early social environment, produces differences in social behavior later in life associated with marked changes of neurotrophin levels in selected brain areas, including hippocampus and hypothalamus.

Key Words: Communal nesting, neurotrophins, maternal behavior, aggressive behavior, psychiatric diseases, early experiences

During early postnatal development, several important processes that shape the mammalian brain are taking place. This highly plastic period characterized by neuronal differentiation, maturation, and synaptogenesis offers the possibility for epigenetic factors to affect brain structure and function (Rosenzweig 2003).

An intact, natural-type, early social environment is crucial for brain and behavioral development, as shown by the disrupting effects of its impoverishment or deterioration (Canetti et al. 1997; Harlow 1958; Pollak 2003; Rutter et al. 1997; Trickett and McBride-Chang 1995). Indeed, children who experience severe perturbations in care are at higher risk for the emergence of behavioral problems, including social behavior (Dodge et al. 1995; Rogosch et al. 1995) or of psychiatric diseases later in life (Dube et al. 2001; Nawa et al. 2000). Manipulations of the mother-infant interaction in rodents have consequences on behavioral and neuroendocrine responses that persist for the entire life-span (Cirulli et al. 2003; Levine 1957; Meaney 2001). For instance, the offspring of rodent mothers exhibiting less care-giving behavior show, at adulthood, an increased response to stressful situations (Liu et al. 1997), producing high levels of adrenal steroids that exert disrupting effects on the nervous system (McEwen 1998).

Neurotrophins, particularly nerve growth factor (NGF) and brain-derived neurotrophic factor (BDNF), are key molecules in neuronal proliferation and differentiation and in synaptogenesis (McAllister et al. 1999) that have been hypothesized to mediate the effects of experience on brain structure and function (Branchi et al. 2004). A series of experiments found that manipulations of the early social environment exert both short- and long-term effects on brain neurotrophin expression in both mice and rats (Cirulli et al. 2003; Liu et al. 2000). A daily 3-hour maternal separation from postnatal day (PND) 2 to PND 14 induces, on PND 17, an increase of NGF and BDNF messenger-RNA expression in the hippocampus and prefrontal cortex of rats (Cirulli et al. 2003; Roceri et al. 2004) and, at adulthood, a selective BDNF reduction in the prefrontal cortex (Roceri et al. 2004). In humans, altered neurotrophin levels have been widely related to several psychiatric disorders, suggesting a role for neurotrophins, particularly BDNF, in the onset and progression of pathologies such as schizophrenia and depression (Castren 2005; Nawa et al. 2000; Schumacher et al. 2005).

The aim of the present work was to characterize the role of early social environment on adult behavior. Communal nesting (CN), the sharing of maternal care-giving behavior among multiple females in a single nest, characterizes the natural ecological niche of developing pups in many rodent species and represents a form of early social enrichment when compared with standard laboratory rearing conditions (Hayes 2000; Sayler and Salmon 1971). We therefore examined the effects of being reared in CN—consisting in three mothers keeping their pups together and sharing care-giving behavior in a single nest—on social/aggressive behavior of offspring at adulthood. Because neurotrophin levels are reportedly modulated by social factors (Aloe et al. 1986; Branchi et al. 2004; Cirulli et al. 2003), we also evaluated whether CN produces long-term changes of NGF and BDNF levels in different brain areas.

Methods and Materials

Animals and Breeding Procedures

Twenty-four male and 48 female mice of an outbred CD-1, Swiss-derived strain (ICR), weighing 25–27 g, were purchased from a commercial breeder (Harlan, Correzzana, Milan, Italy). Upon arrival at the laboratory, the animals were housed in an...