Neuropharmacology 58 (2010) 78–87

Contents lists available at ScienceDirect

Neuropharmacology

journal homepage: www.elsevier.com/locate/neuropharm

Maternal separation interferes with developmental changes in brain vasopressin and oxytocin receptor binding in male rats

M. Lukas, R. Bredewold, I.D. Neumann, A.H. Veenema*

Department of Behavioral Neuroendocrinology, University of Regensburg, Regensburg, Germany

ARTICLE INFO

Article history:
Received 25 May 2009
Received in revised form
15 June 2009
Accepted 17 June 2009

Keywords:
Development
Early life stress
V_{1A} receptor
Septum
Ventromedial hypothalamus

ABSTRACT

Brain vasopressin V_{1A} receptors (V_{1A}-R) and oxytocin receptors (OT-R) are important modulators of social behaviors. We recently showed that exposure to maternal separation (MS; 3 h daily, postnatal days 1–14) induces changes in social behaviors in juvenile and adult male rats. Here, we hypothesize that MS induces brain region-specific changes in V_{1A}-R and OT-R across development, which in turn, may underlie MS-induced changes in social behaviors. We examined the effects of MS on V_{1A}-R and OT-R binding in forebrain regions of juvenile (5 weeks), adolescent (8 weeks), and adult (16 weeks) male rats. Robust age-related changes were found for V_{1A}-R and OT-R binding in several brain regions. For example, in the lateral septum V_{1A}-R binding increased while OT-R binding decreased with age. Most notably, OT-R binding in the caudate putamen showed a 2-fold decrease while OT-R binding in the ventromedial hypothalamus showed a 4-fold increase with age. Importantly, exposure to MS interfered with these developmental changes in several brain regions. Specifically, MS significantly increased V_{1A}-R binding in the piriform cortex (at adolescent and adult ages), the lateral septum (at juvenile age), the hypothalamic attack area (at adolescent age), and the dentate gyrus of the hippocampus (at adolescent age), and decreased V_{1A}-R binding in the arcuate nucleus (at juvenile age). Moreover, OT-R binding was significantly lower in the agranular cortex (at juvenile and adolescent age), the lateral septum (at adult age) and the caudate putamen (at adult age), but higher in the medial preoptic area (at adolescent age) and ventromedial hypothalamus (at adult age) after exposure to MS. In conclusion, age-dependent changes in V_{1A}-R and OT-R binding are likely associated with the maturation of behaviors, such as sexual and aggressive behaviors, while disruption of these changes by MS might contribute to previously observed changes in social behaviors after MS.

© 2009 Elsevier Ltd. All rights reserved.

1. Introduction

The neuropeptides arginine vasopressin (AVP) and oxytocin (OT) are key players in the regulation of a wide variety of social behaviors, including aggression, affiliation, sexual behaviors, and social cognition, in both humans and animals (for reviews see Engelmann et al., 1996; Lim and Young, 2006; Caldwell et al., 2008; Goodson, 2008; Heinrichs and Domes, 2008; Veenema and Neumann, 2008). The behavioral effects of AVP and OT are mediated by their respective receptors, the AVP V_{1A} receptor (V_{1A}-R), the V_{1B}-R, and the OT receptor (OT-R). Due to its wide-spread distribution in the brain compared with the more restricted distribution of the V_{1B}-R, the V_{1A}-R is thought to be the predominant AVP receptor in the brain (Tribollet et al., 1988; Ostrowski et al., 1994; Vaccari et al., 1998). Interestingly, V_{1A}-R and OT-R undergo brain region-specific changes in expression throughout development (Tribollet et al., 1989, 1991), suggesting that these neuropeptide receptors play a role in the maturation of social behaviors. Moreover, large variations in brain V_{1A}-R and OT-R expression and binding density are observed in closely related species that show distinct social structures (Insel et al., 1991; Barberis and Tribollet, 1996; Young et al., 1996, 1997; Goodson and Bass, 2001), and even between individuals of the same species (Phelps and Young, 2003; Olazabal and Young, 2006). These findings suggest that variations in V_{1A}-R and OT-R binding might contribute to variations in social behaviors.

Negative early life experiences have been associated with robust alterations in social behaviors. Among them, child maltreatment is an acknowledged risk factor for the development of excessive aggression and violence (Widom, 1989; Dodge et al., 1990; Barnow and Freyberger, 2003; Fonagy, 2004). Changes in aggressive behaviors were also found in virtually all primate and rodent models of early life stress (reviewed in Veenema, in press). One of

* Corresponding author. Present address: Dept. of Psychology, University of Massachusetts, Tobin Hall, Amherst, MA 01003, USA. Tel.: +1 413 545 4309; fax: +1 413 545 0996.
E-mail address: aveenema@psych.umass.edu (A.H. Veenema).

0028-3908/$ – see front matter © 2009 Elsevier Ltd. All rights reserved.
doi:10.1016/j.neuropharm.2009.06.020

the most frequently used models of early life stress, maternal separation (MS) of rat or mouse pups, induces long-lasting alterations in anxiety- and depression-like behaviors and in neuroendocrine correlates (Plotsky and Meaney, 1993; Wigger and Neumann, 1999; Kalinichev et al., 2002; Romeo et al., 2003; Ladd et al., 2004). We recently demonstrated that exposure to MS alters intermale aggression in rats and mice (Veenema et al., 2006, 2007). These alterations were already evident early in development, as demonstrated by increased aggressive behaviors during play-fighting in 5-week-old juvenile male rats (Veenema and Neumann, 2009). Based on these findings we proposed that brain systems involved in social behaviors, like the AVP and OT systems, are changed by MS. Indeed, MS increased AVP mRNA expression in the hypothalamic paraventricular nucleus (PVN) in both juvenile and adult male rats (Veenema et al., 2006; Veenema and Neumann, 2009), suggesting consistent alterations across development. However, MS-induced alterations in other parameters were less consistent as for example, MS increased corticotropin-releasing hormone mRNA expression in the PVN in response to the resident-intruder test in adolescent and adult, but not in juvenile, rats (Veenema, in press). These findings elucidate the importance of studying early life stress-induced alterations in neurobiological parameters in view of developmental changes.

Given the important role for V_{1A}-R and OT-R in the regulation of social behaviors, the question arises whether MS alters V_{1A}-R and OT-R binding density in the brain and if so, whether these changes are stable throughout development. We used receptor autoradiography to measure the effect of MS on V_{1A}-R and OT-R binding in forebrain regions in juvenile, adolescent, and adult male rats. Identifying changes in V_{1A}-R and/or OT-R binding density after exposure to MS may generate new hypotheses as to which brain regions are likely involved in the previously observed MS-induced changes in social behaviors.

2. Methods

2.1. Animals

After one week of habituation in our laboratory facility, Wistar rats (Charles River, Sulzfeld, Germany) were mated for five days. During the last week of gestation, female rats were individually housed in standard rat cages (42 × 27 × 18 cm), and maintained under standard laboratory conditions (12:12 light:dark cycle, lights on at 6:00 A.M., 22 °C, 60% humidity, food and water ad libitum). The experimental protocols were approved by the Committee on Animal Health Care of the government of Oberpfalz and conformed to the international guidelines on the ethical use of animals.

2.2. MS procedure

MS was performed as described earlier (Veenema et al., 2006). Briefly, on the day after parturition, i.e. on postnatal day 1, each litter was culled to eight – 10 pups (each litter contained six to eight males and two to four females). Pups were separated from the mother for 3 h daily between 9:00 A.M. and noon from postnatal

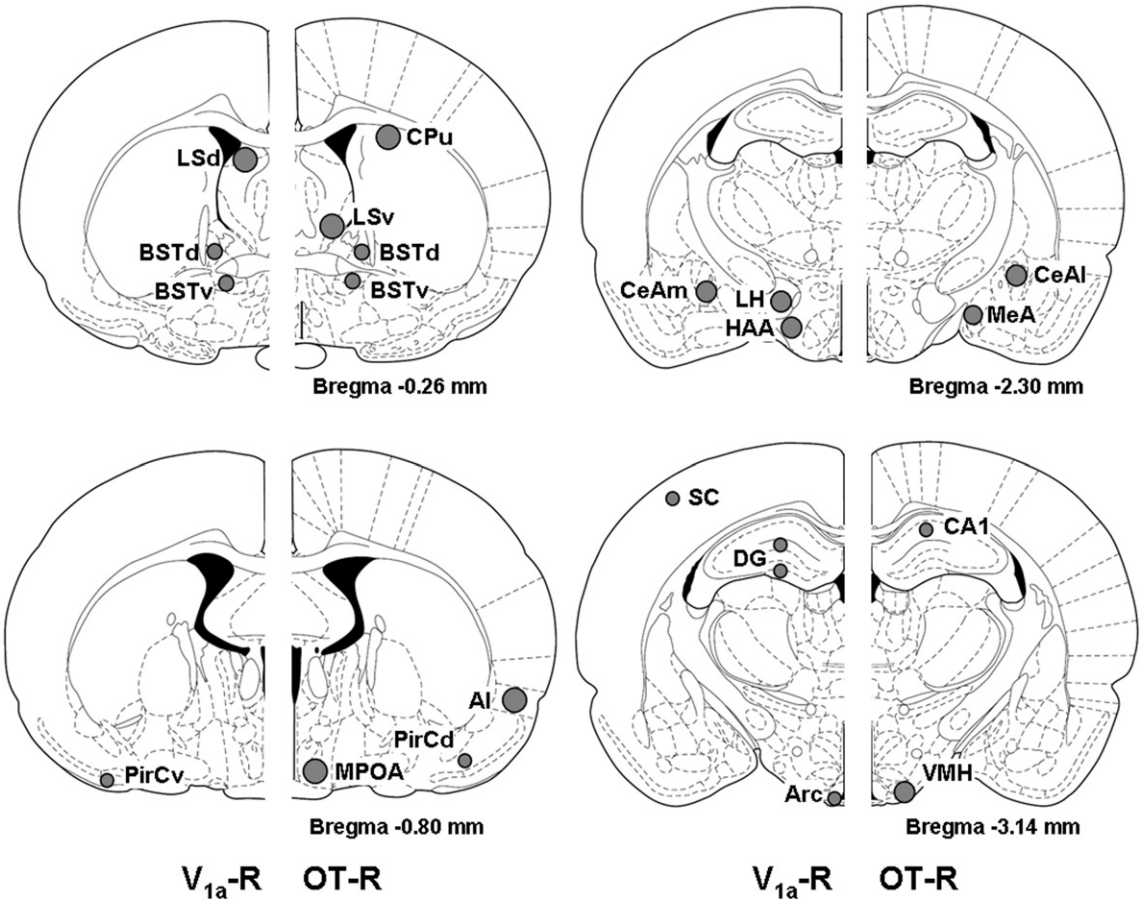

Fig. 1. Schematic diagrams (adapted from the atlas of Paxinos and Watson , 1998) of the brain regions in which vasopressin V_{1A} receptor (V_{1A}-R) and oxytocin receptor (OT-R) binding were quantified in 5-, 8-, and 16-week-old male control and maternally separated rats. AI, agranular insular cortex; Arc, arcuate nucleus; BSTd, bed nucleus of the stria terminalis dorsal; BSTv, bed nucleus of the stria terminalis ventral; CA1, CA1 region of the hippocampus; CeAl, central amygdala lateral, CeAm central amygdala medial; CPu, caudate putamen; DG, dentate gyrus of the hippocampus; HAA, hypothalamic attack area, LH, lateral hypothalamus; LSd, lateral septum dorsal; LSv, lateral septum ventral; MeA, medial amygdala; MPOA, medial preoptic area; PirCd, piriform cortex dorsal; PirCv, piriform cortex ventral; SC, primary somatosensory cortex; VMH, ventromedial hypothalamus.

Download English Version:

https://daneshyari.com/en/article/2494173

Download Persian Version:

https://daneshyari.com/article/2494173

Daneshyari.com