

Vasopressin and oxytocin receptor mRNA expression during rat telencephalon development

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Summary We investigated the developmental expression of vasopressin and oxytocin receptor and peptide mRNA using semi-quantitative reverse transcription-polymerase chain reaction (RT-PCR) and Southern blot hybridization. Messenger RNAs for both vasopressin receptor subtypes V_{1a} and V_2 were present in the telencephalon from embryonic day 12 to day 20. Both V_{1a} and V_2 receptor mRNA increased on day 13 and then remained stable from embryonic day 13 to day 20. Messenger RNA for the vasopressin peptide was also detected in the telencephalon from day 12 to day 20, indicating that vasopressin could be synthesized within the rat cerebral cortex during rat embryonic development. Oxytocin receptor mRNA expression was also present in the telencephalon, but expression levels varied considerably from day 12 to day 20. No oxytocin mRNA expression was detected during rat telencephalon development. Temporal patterns of vasopressin receptor and vasopressin peptide mRNA expression along with oxytocin receptor mRNA suggest a temporal role for vasopressin- and oxytocin-mediated actions during rat telencephalon development. © 2000 Harcourt Publishers Ltd

INTRODUCTION

Vasopressin (VP) and oxytocin (OT) are two closely related neuropeptides implicated in various brain functions including learning and memory (Chen et al., 1996). VP-like and OT-like immunoreactive fibers are widely present in the central nervous system (Brinton et al., 1994b; Buijs et al., 1980). VP mRNA expression has been detected in the amygdala by *in situ* hybridization (Szot et al., 1994) and in the cerebral cortex and hippocampus by Northern blot analysis (Buijs, 1992; De Wied et al., 1993). OT mRNAs have not been detected in the cerebral cortex (De Wied et al., 1993). During embryonic development, VP, OT and their associated neurophysins have been detected in the rat brain as early as fetal day 14 (Buijs, 1980; Rozen et al., 1995; Tribollet et al., 1992). However, VP and OT peptide mRNA expression patterns during rat telencephalon development have not been reported.

VP exerts its functions through three VP receptor subtypes ($V_{1a}R$, $V_{1b}R$, and V_2R) whereas OT exerts its function through one known OT receptor type (OTR). These receptors have been demonstrated by gene cloning, sequencing and functional expression, and have been characterized by their binding properties and second messenger effectors (For reviews, see Burbach et al., 1995; Barberis and Tribollet, 1996). Our discovery of VP recognition sites in cerebral cortex of the adult male rat by radioisotope-labeled ligand binding more than a decade ago (Brinton et al., 1984) has been confirmed by a number of laboratories (Chen et al., 1993; Johnson et al., 1993; Tribollet et al., 1992). More recent studies have detected $V_{1a}R$ mRNA expression in the adult cerebral cortex by *in situ* hybridization (Ostrowski et al., 1994; Szot et al., 1994) and RT-PCR (Hirasawa et al., 1994; Yamazaki et al., 1997). $V_{1b}R$ mRNA has also been detected in the adult rat cerebral cortex and hippocampus by RT-PCR (Lolait et al., 1995). Functional expression of V_2 receptor in embryonic neurons was reported by Brinton and Brownson (Brinton and Brownson, 1993) where VP transiently induced cAMP formation in cultured hippocampal neurons. Later studies by Hirasawa et al. (Hirasawa et al., 1994) and Kato et al. (Kato et al., 1995) showed that V_2R mRNAs were present in the cerebral cortex of newborn but not adult rats. Radio-labeled

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ligand binding studies were first detected VP recognition sites in the cerebral cortex and hippocampus as early as postnatal day one (Snijidewint et al., 1989). Expression of VP receptor mRNA during telencephalon development has not been previously reported.

OT-binding sites have been detected in various brain regions including the cerebral cortex and hippocampus in the adult by radio-labeled ligand studies (Tribollet et al., 1992; Klein et al., 1995). Developmentally, OT recognition sites have been detected in the cerebral cortex in the early postnatal development by radio-labeled ligand binding studies (Sinding et al., 1980; Petracca et al., 1986). The earliest appearance of OT binding sites in the cerebral cortex and hippocampus were observed at postnatal day 1 (Snijidewint et al., 1989). OTR mRNAs have been detected in the adult rat brain (Yoshimura et al., 1993) including various cortical structures such as the anterior olfactory nucleus and the bed nucleus of the stria terminalis. OTR mRNA expression has been observed in the brain as early as E13 (specifically, primordium of the dorsal motor nucleus of vagus), and the cerebral cortex at E20 and in the cingulate cortex at postnatal day 1 (Yoshimura et al., 1996). OTR mRNA expression has not been found in the telencephalon earlier than E20.

To resolve whether the sites detected in cortex were present in neural tissue or were vascular in origin we selectively cultured neurons, astroglia, oligodendrocytes and determined the presence of V_1a receptor mRNA in each of the cell types. Results of RT-PCR analysis demonstrated that mRNA for V_1aR was expressed in neurons, astroglia, oligodendrocytes derived from embryonic rat brain (Yamazaki et al., 1997). To determine whether the V_1a receptors in these cell types were functional, we investigated the signal transduction pathway activated by selective V_1R agonists. We further investigated whether activation of these receptors mediated a cellular response. Results of these studies demonstrated VP-induced calcium signaling (Brinton et al., 1994a; Son and Brinton, 1998) and VP-induced neurotrophism in cultured cortical and hippocampal neurons (Brinton et al., 1994b; Chen et al., in press). These studies conducted with embryonic cultured neurons suggested to us that VP and OT might play a role during cerebral cortex development. To pursue this postulate, we have investigated expression of VP and OT receptor and peptide mRNAs in telencephalon development using semi-quantitative RT-PCR and Southern blot analysis.

MATERIALS AND METHODS

Tissue materials

The telencephalon region including the cerebral cortex and the hippocampus derived from E12 to E20 rat fetal brains was dissected (shown in Fig. 1). Brain tissue from

10–14 rat fetal brains were pooled and used for total RNA isolation. Total RNAs from the plant *Lolium Perenne* (grass) were selected as a negative control to avoid contamination of vascular derived V_1aR since all organs that might be V_1aR negative are nevertheless innervated by the vascular system that contains the V_1aR . Total RNAs from the frontal, occipital, parietal, and temporal regions of the adult rat cerebral cortex and from the dorsal and ventral regions of the hippocampus were also isolated.

RT-PCR

Total RNAs were isolated from the telencephalon region described above using RNA STAT-60 kit (TEL-TEST 'B', Inc., Texas, USA). The RNA concentration was determined by spectrophotometry. Reverse transcription reactions were performed for each RNA sample using 1 μ g of total RNA in reverse transcription buffer composed of 10 mM DTT, 20 μ M each of dATP, dCTP, dGTP, and dTTP, and 1 μ M of oligo(dT)₁₅₋₁₈ (Yamazaki et al., 1997). The solution was heated to 65°C for 5 min and cooled to 37°C for 10 min, and then 25 units of AMV reverse transcriptase was added. After incubation at 37°C for 1 h, the mixture was heated to 95°C for 5 min prior to storage at -20°C.

Master mixes for PCR reaction were used for each sample. The PCR reaction mixture contained forward and reverse primers (10–20 pmol each), dNTPs (200 μ M each as final concentration), 10 \times PCR buffer, Taq DNA polymerase (0.5 units) (Boehringer-Mannheim Inc., Indiana, USA), 1 μ l of the RT mixture as the source of cDNA. The primers used for PCR reaction were as follows: (1) 5'TAC GTG ACC TGG ATG ACC AG3' (nt 901–920) (forward) and 5'AGC AAC GCC GTG ATT GTG AT3' (nt 1255–1275) (reverse) for V_1a receptor cDNA fragment (Morel et al., 1992); (2) 5'TGA CAC TAG ACC GCC ATC GT 3' (nt 439–458) (forward) and

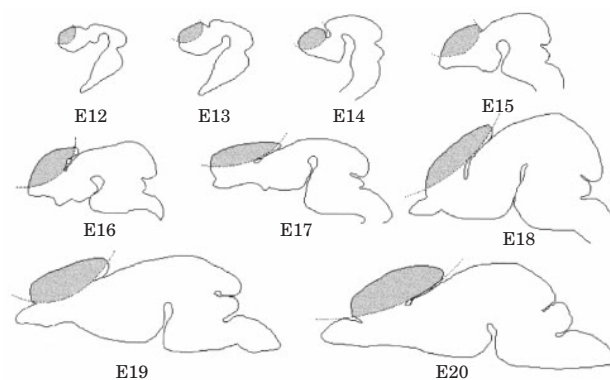


Fig. 1 Sagittal view of prenatal rat brain during development. The shadowed areas represent the telencephalic region which were dissected and collected for total RNA isolation. Modified from Altman and Bayer (1995).

5'GGC ACC AGA CTG GCG TGT AT3' (nt 735–754) (reverse) for V₂ receptor cDNA fragment (Lolait et al., 1992) (3) 5'ACA TCA CCT TCC GCT TCT AT3' (nt 3482–3501); (forward) and 5'TTG AAG CTG ATG AGG CCG TA3' (nt 3841–3860) (reverse) for OTR cDNA fragment (Rozen et al., 1995); (4) 5'CAC TAC GCT CTC TGC TTG CCT CC3' (nt 41–63) (forward) and 5'AGA ATC CAC GGA CTC TTG TGT CC3' (nt 484–506) (reverse) for VP peptide cDNA (Rehbein et al., 1996); (5) 5'TCA CCG ACG GTG GAT CTC GGA CT 3' (nt 1–23) (forward) and 5'CTC GGA GAA GGC AGA CTC AGG GTC3' (nt 385–408) (reverse) for OT peptide cDNA (Rehbein et al., 1996); (6) β-Actin was used as a semi-quantitative control and the primer set was purchased from Stratagen Inc. Amplification was performed at 94°C for 40 seconds, 56°C for 1 min, and 72°C for 1 min, for 35 cycles. The PCR reaction of water with primers was also conducted as a control. After amplification, each sample was electrophorased on a 1.5% agarose gel and transferred onto a nylon membrane for DNA hybridization.

Southern blot hybridization

The cDNA clones of V_{1a} and V₂ receptor, and OT receptor were kindly provided by Dr Stephen Lolait of NIH. VP and OT peptide cDNA clones were kindly provided by Dr Joseph A. Majzowb of Harvard University and Dr Alan C. Watts of USC. Radio-labeled cDNA probes were made using an oligo-labeling kit from Pharmacia Inc. (New Jersey, USA). Southern blot hybridization was performed as follows: The filters were prehybridized in prehybridization solution (50% formamide, 2 × Denhardt's solution (0.04% of Ficoll, 0.04% of polyvinylpyrrolidone, and 0.04% of BSA), 4 × SSC (3.5% of NaCl and 1.76% of sodium citrate, pH 7.0), 0.1% SDS and 100 µg/ml salmon sperm DNA) at 42°C for 2 h. Hybridization reaction was carried out by adding 10⁶ cpm/ml of the denatured probe in new pre-hybridization buffer. After hybridization, the filter was washed by 1 × SSC, 0.4% SDS at room temperature for 30 min once and 0.3 × SSC, 0.4% SDS at 68°C for 30 min twice. The filter was immediately wrapped with Saran paper, inserted into autoradiographic cassette and exposed to X-ray film for 2–4 h.

RESULTS

Expression of VP and OT receptor mRNAs in the developing rat telencephalon

Five brain vesicles (the telencephalon, the diencephalon, the mesencephalon, the metencephalon, and the myelencephalon) are present at embryonic days 11–12 (Fig. 1). The cerebral hemispheres are present at embryonic day 12–13 (Figure 1). Total RNAs were isolated from the telencephalon region or the cerebral cortex (including the

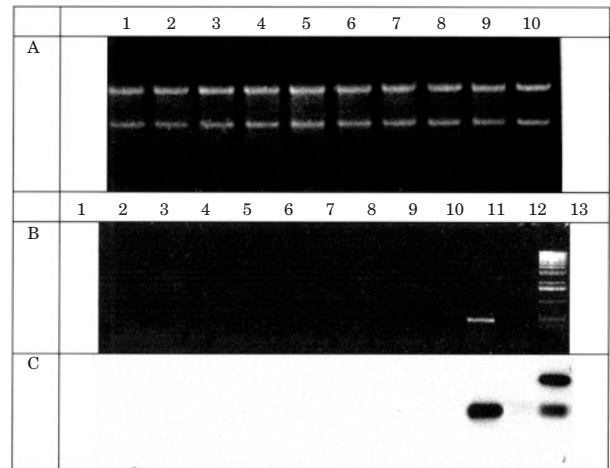


Fig. 2 Negative controls for PCR. Total RNA samples were isolated from the telencephalon region of rat fetal brains and used for direct PCR reactions without reverse transcription (RNA-PCR). A: ethidium bromide-stained total RNA samples from the telencephalon region of E12, E13, E14, E15, E16, E17, E18, E19 and E20 rat fetal brains respectively (lanes 1 to lane 9) and from *Lolium Perenne* (lane 10). B: agarose gel electrophoresis of RNA-PCR reactions. The V_{1a}R primer set was used. Lane 1, water-control; Lane 2 to lane 10: samples from E12 to E20 respectively. Lane 11, the cDNA transcribed from E18 total RNA; Lane 12, the PCR product of *Lolium Perenne* RNA; Lane 13, 1 kb ladder. C: Southern blot hybridization of B using ³²P-labeled V1aR probe.

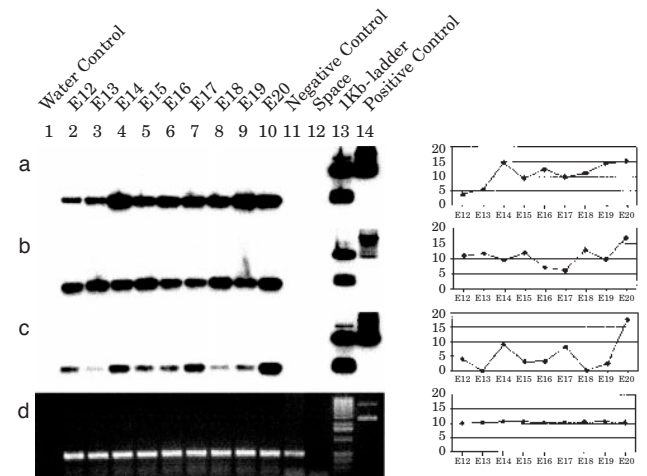


Fig. 3 Expression of vasopressin and oxytocin receptor mRNAs during rat telencephalon development. Total RNAs were isolated from the telencephalon region dissected from E12 through E20 rat fetuses and subjected to semi-quantitative RT-PCR and Southern blot analysis. A: V_{1a}R mRNA expression pattern; B: V₂R mRNA expression pattern; C: OTR mRNA expression pattern; D: Actin control. Lane 1: Water-control; Lane 2 to 10: The telencephalon region derived from E12, E13, E14, E15, E16, E17, E18, E19, and E20 rat fetal brains respectively. Lane 11: Negative control (*Lolium Perenne*); Lane 12: Space; Lane 13: 1Kb-ladder; Lane 14: Positive control (Plasmid). Optical density photometry of the Southern blots were conducted on both the receptor and actin Southern blots. Relative quantitation for levels of V_{1a}R, V₂R and OxyR mRNA expression were normalized to the level of actin mRNA.

hippocampus) of rat fetal brains from embryonic day 12 to day 20 and measured by spectrophotometry (Fig. 2). An equal amount of each total RNA sample was used for RT-PCR reactions (Fig. 2). To ensure the specificity of amplification, direct amplification of total RNA samples without RT-reactions did not show any bands in agarose gels as well as Southern Blot analysis (Fig. 2, panels B and C). No amplified bands appeared when cDNA templates were excluded from the amplification reaction (Fig. 2, lane 1).

Following determination of the specificity of PCR amplification, reverse transcription PCR was performed. The amplified cDNAs from RT-PCR reactions were transferred onto nylon membranes and hybridized with V_1aR , V_2R and OTR cDNA probes respectively. Hybridization results demonstrated the presence of both V_1aR and V_2R mRNAs in the cerebral cortex, including the hippocampus, throughout the developmental time frame investigated, from day 12 to day 20 (Fig. 3). Optical density photometry of the Southern blots were conducted on both the receptor and actin Southern blots and relative quantitation for levels of V_1aR , V_2R and OTR mRNA expression were normalized to the level of actin mRNA (Fig. 3, panels A–D). Messenger RNA for the V_1aR was detected at the earliest time point, embryonic day 12 and was consistently expressed throughout embryonic development. Expression levels for V_1aR mRNA increased at day 14 relative to days 12 and 13 and remained elevated throughout the time frame investigated (Fig. 3, panel A). V_2R mRNA was detected at the earliest time point, embryonic day 12 and remained at the same level of expression until embryonic day 16 when the levels plummeted and then rebounded at embryonic day 18 and reached the highest level of expression on embryonic day 20 (Fig. 3, panels B). The expression pattern for OTR was much more variable than that for the vasopressin receptors. OTR mRNA was detectable at embryonic day 12, was undetectable at day 13, then resurged at day 14, declined at embryonic days 15 and 16 and was undetectable again at embryonic day 18 and then showed a 3–4-fold rise in expression at embryonic day 20 (Fig. 3, panel C). Actin mRNA expression remained consistent across the time frame investigated. The invariant actin mRNA expression was used as a semi-quantitative control and *Lolium Perenne* mRNA was used as a negative invariant control.

Expression of VP and OT peptide mRNAs in the developing telencephalon and the adult rat cerebral cortex and hippocampus

Having determined the presence of V_1a , V_2 and OT receptors in the developing brain, we pursued whether the mRNAs for the endogenous ligands for these receptors were also present during the same developmental time points. We investigated VP and OT peptide mRNA expression in rat telencephalon development

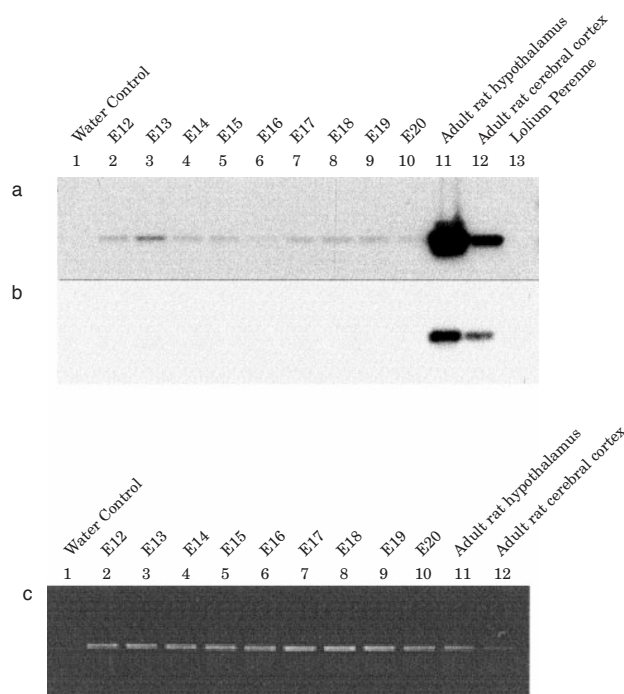


Fig. 4 Expression of vasopressin and oxytocin peptide mRNAs during rat telencephalon development. Total RNAs were isolated from the rat telencephalon region dissected from E 12 through E 20 rat fetuses and subjected to semi-quantitative RT-PCR and Southern blot analysis. A: Vasopressin mRNA expression; B: Oxytocin mRNA expression; C: Actin control. Lane 1. Water-control; Lanes 2–10: The telencephalon region derived from E12, E13, E14, E15, E16, E17, E18, E19, and E20 rat fetus brains respectively. Lane 11: Adult rat hypothalamus; Lane 12: Adult rat cerebral cortex; Lane 13: *Lolium Perenne* as a negative control.

using semi-quantitative RT-PCR and Southern blot analysis (Fig. 4). VP peptide mRNA was present in the telencephalon throughout the developmental time frame investigated, from day 12 to day 20, whereas no OT peptide mRNA expression was detected. The expression level of VP peptide mRNA was very low compared to the expression levels of V_1aR and V_2R . Both VP and OT peptide mRNAs were expressed in the adult rat hypothalamus as expected, and also in the adult rat cerebral cortex. The data indicate that VP peptide mRNA is uniquely expressed within the rat cerebral cortex during rat embryonic development whereas both VP and OT peptide mRNAs are present in the mature adult rat cortex.

Regional patterns of VP and OT receptor mRNA expression in the adult cerebral cortex and hippocampus

To determine regional patterns of VP and OT receptor mRNA expression in the adult cerebral cortex and hippocampus we used semi-quantitative RT-PCR and Southern blot analysis. Results of these analyses are

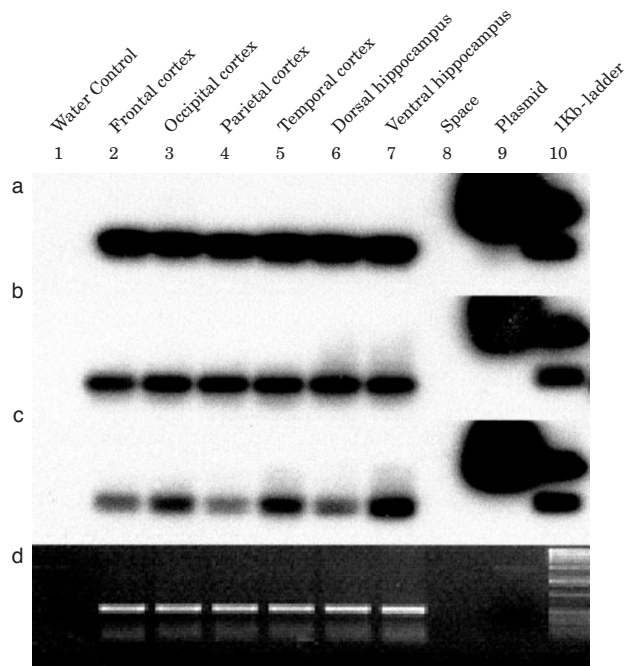


Fig. 5 Regional patterns of vasopressin and oxytocin receptor mRNA expression in the adult rat cerebral cortex and hippocampus. A: V_1a vasopressin receptor mRNA expression; B: V_2 vasopressin receptor mRNA expression; C: Oxytocin receptor mRNA expression; D: Actin control. Lane 1: Water-control; Lanes 2–5: Frontal, occipital, parietal and temporal regions of the cerebral cortex respectively; Lanes 6–7: The dorsal and ventral regions of the hippocampus respectively; Lane 8: Space; Lane 9: Positive control (plasmid); Lane 10: 1Kb-ladder.

shown in Figure 5. V_1aR , V_2R and OTR mRNAs were expressed in all four regions of the adult rat cerebral cortex (frontal, occipital, parietal, and temporal regions) and in two areas of the adult rat hippocampus (dorsal and ventral parts). The data suggest a broad distribution of VP and OT receptors in the cerebral cortex regardless of subtype.

DISCUSSION

Vasopressin and oxytocin receptor mRNA expression throughout entire rat telencephalon development

To elucidate the functional roles of vasopressin and oxytocin receptor expression during prenatal rat telencephalic development, we have first investigated the expression of VP receptor and OT receptor mRNA in the rat telencephalon from embryonic day 12 to day 20 using RT-PCR and Southern blot analysis. Results of these studies demonstrate that V_1aR , V_2R and OTR mRNAs are each expressed in the rat telencephalon throughout the time frame studied. Expression levels for both V_1a and V_2 receptor mRNAs were increased on day 13 and differed only slightly from embryonic day 13 to

day 20. Since five brain vesicles are apparent in the rat embryonic day 11 brain and the telencephalon can only be distinguished from the diencephalon, the mesencephalon, the metencephalon, and the myelencephalon on embryonic days 11–12, this time frame covers the entire telencephalon prenatal time course.

By comparison, the mRNA expression pattern of OTR during rat telencephalon development was different from that of the V_1aR and V_2R . OTR mRNA expression was detected in the telencephalon from embryonic day 12 to day 20, with expression levels varying considerably from day 12 to day 20 whereas V_1aR and V_2R mRNAs showed relative consistent expression throughout this time frame. The variation in OTR mRNA expression may be due to transient expression in one region or to differential expression in select areas of the cerebral cortex. Transient expression of OTR mRNAs and no expression of OT peptide mRNAs during telencephalon prenatal development suggest that OT does not consistently function during the telencephalon prenatal development.

Evidence for Functional Expression of Vasopressin Receptor During Rat Telencephalon Development

The presence of receptor mRNA does not prove the presence of receptor protein. Thus, one can question whether the mRNAs for VP and OT receptor are translated into the proteins and whether these receptor proteins are functional. Radioligand binding studies have indicated that VP receptor expression is first detectable at postnatal day one (Snijidewint et al., 1989) and the earliest day for OTR mRNA expression in the cerebral cortex was reported to be at E20 (Yoshimura et al., 1996). In contrast, the present data indicate that the mRNAs for VP and OT receptors are present much earlier in embryonic development. Functional analyses have demonstrated VP-induced neurotrophism (Brinton et al., 1994b; Chen et al., in press) and calcium signaling (Brinton et al., 1994a; Son and Brinton, 1998) in embryonic day 18 cultured neurons derived from the cerebral cortex and hippocampus. These data indicate that the VP receptors in the late stages of neo- and palio-cortex embryonic development are indeed functional and demonstrate that the mRNA detected at this point in development is translated into functional receptor protein. Functional analyses of VP and OT receptor at earlier stages of development are ongoing in our laboratory.

Neurotransmitter receptors are essential for functions of cerebral cortical neuronal circuitry and have been implicated in regulation of different aspects of corticogenesis (Lidow and Wang, 1995). If VP receptors are functional during earlier neo-cortical development, then one would expect to see abnormalities in the brain deficient in vasopressin. Boer and colleagues (Boer et al., 1982)

reported some time ago impaired cerebral cortex development in the diabetes insipidus Brattleboro rat. In the homozygous Brattleboro rat, a decrease in the weight, lipid content and DNA content of cerebral cortex was observed (Boer et al., 1982). The Brattleboro diabetes insipidus rat has a single base deletion in the vasopressin gene, which prevents accurate translation of the VP peptide (Schmale and Richter, 1984). Our data demonstrating the presence of VP receptor mRNA expression in the cerebral cortex and its neurotrophic action may provide some insight into the deficits found in the VP deficient Brattleboro rats.

While correlational in nature, the co-expression of both VP receptor mRNAs and VP peptide mRNAs in cortex suggests the coordinate development of VP signaling system during telencephalic development. The same coordinate pattern was not apparent for the OT receptor mRNA and OT peptide mRNA signaling system. The remarkable absence of oxytocin peptide mRNA throughout development was surprising. The absence of oxytocin peptide mRNA stands in contrast to the high levels of oxytocin in the maternal plasma during parturition. This remarkable contrast remains to be confirmed by other investigators and its significance determined. It is possible that because vasopressin discriminates poorly between VP and OT receptors such that [³H]-VP can label OT receptors nearly as efficiently as VP receptors (Dreifuss and Raggenbass, 1993), vasopressin could be activating both VP and OT receptors. It is also possible that VP and OT responsive cells during early telencephalic development may not be fully differentiated during embryonic development allowing VP to activate both VP and OT receptors. The distinction between the development of these two signaling pathways provides a unique opportunity to address the functional role of these two closely related signaling pathways on telencephalon development. We are currently pursuing this question.

Difference of vasopressin receptor mRNA expression in the telencephalon between embryonic stage and adulthood

Differences in mRNA expression levels in the telencephalon between the embryonic and the adult brain were also observed in the present studies. V₁aR, V₂R and OTR mRNAs were broadly expressed in the frontal, occipital, parietal, and temporal regions of adult cerebral cortex and in the dorsal and central regions of hippocampus. These data have further confirmed earlier radioligand binding results indicating broad distributions of VP recognition sites in the adult cerebral cortex and hippocampus (Brinton et al., 1984; Chen et al., 1993; Johnson et al., 1993; Tribollet et al., 1992) However, the expression level

for V₁aR mRNAs in the telencephalon was higher in the adult than during the embryonic stages investigated. This observation is consistent with other reports which have suggested that expression of VP and OT binding sites increased during the course of development (Snijidewint et al., 1989). The increased V₁aR mRNA expression level of the adult brain could be due to increased V₁aR mRNA expression in adult neurons than during development. Alternatively, the increased V₁aR mRNA expression level of the adult brain could be due to a higher expression level in glia cells than in neurons. Our earlier data demonstrated that mRNA for V₁aR was expressed in neurons and glia cells derived from embryonic rat cerebral cortex (Yamazaki et al., 1997). V₂R mRNA expression has not been confirmed in glia cells. Consistent expression of V₂R mRNA demonstrated in the present study stands in contrast to the earlier evidence that V₂R was only transiently expressed during early postnatal development and disappeared later (Brinton and Brownson, 1993; Hirasawa et al., 1994). The continued expression of V₂R mRNA into adulthood raises the possibility that V₂R protein may still be expressed.

Different expression of vasopressin and oxytocin peptide mRNAs during rat telencephalon development

Since VP and OT receptor mRNA were present in the developing cerebral cortex, we sought to determine whether VP and OT peptide expression patterns were coincident with receptor expression. To address this issue, we investigated VP and OT peptide mRNA expression patterns during rat telencephalon development. VP peptide mRNA was present in the telencephalon from embryonic day 12 to day 20 at a low but invariant expression level. In contrast, no OT peptide mRNA expression was detected during the same time frame of rat telencephalon development. The lower level of VP peptide mRNA expression compared to its receptor mRNA expression suggests that the VP peptide may be synthesized sparsely within the cerebral cortex or in select cortical areas during rat embryonic development. These data suggest too that neurons could be directly innervated by VP but not OT in the developing telencephalon. The different mRNA expression patterns between these peptides may indicate different functions of VP and OT during rat telencephalon development. In contrast, both VP and OT peptide and receptor mRNAs were expressed in the adult rat cerebral cortex, which showed different patterns in the adult telencephalon compared to those during the embryonic development.

CONCLUSION

In conclusion, V₁aR, V₂R, and OT receptor mRNAs were each expressed during rat telencephalon development

and exhibited unique expression patterns. VP peptide mRNA was expressed throughout rat telencephalon development whereas no OT mRNA was detected at the same time points. In contrast, in the adult cerebral cortex and hippocampus the mRNAs for both VP and OT peptides, and for V₁aR, V₂R and OTR were consistently present. The differential expression of VP and OT neuro-peptide mRNA expression and that of their cognate receptors provide a foundation upon which to further pursue their functional relevance in the development of cortical structures involved in memory function.

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