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Research Report

Assessment of attention in male and female Brattleboro rats using a self-paced five-choice serial reaction time task

Michael D. Berquist II[a], Sean M. Mooney-Leber[a], David Feifel[b], Adam J. Prus[a,*]

[a]Psychology Department, Northern Michigan University, Gries Hall, 1401 Presque Isle Avenue, Marquette, MI 49855, USA

[b]Department of Psychiatry, University of California, San Diego, San Diego, CA, USA

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ABSTRACT

The Brattleboro rat is a mutant variation of the Long–Evans strain that exhibits negligible central nervous system levels of vasopressin, a neuropeptide that may influence behavioral and cognitive processes. Compared to Long–Evans rats, Brattleboro rats exhibit diminished fear conditioning and have impairments in spatial memory and sensory gating. The present study sought to further evaluate the cognitive profile of vasopressin-deficient rats by studying attention in male and female Brattleboro and heterozygous rats using a self-paced version of the five-choice serial reaction time task. Male Brattleboro rats required significantly more sessions to meet the training criteria than those by heterozygotic and Long–Evans (wild type) rats. Female Brattleboro rats displayed significantly poorer attention accuracy compared to heterozygotic and Long–Evans rats. Taken together, the present findings add further evidence that vasopressin deficiency diminishes cognitive functioning.

1. Introduction

Vasopressin is a neuropeptide that is synthesized primarily in the paraventricular and supraoptic nuclei of the endocrine hypothalamus and released from the pituitary gland into blood circulation. The main physiological functions of vasopressin are the regulation of kidney water retention in response to alterations in blood osmolality (e.g., Dunn et al., 1973) and vasoconstriction in response to changes in hemodynamics, such as arterial hemorrhage (e.g., Pittman et al., 1982). In addition, receptors for vasopressin are located in several brain regions, including the amygdala and hippocampus (e.g., Buijs, 1980; De Kloet et al., 1985), and thus vasopressin may have functional roles in the central nervous system such as altering stress response mechanisms (e.g., see Volpi et al., 2004 and Aguilera, 1994), influencing aspects of social behavior (Donaldson and Young, 2008), and possibly mediating disorders such as depression and schizophrenia (De Wied and Sigling, 2002).

Many behavioral studies in the vasopressin-deficient Brattleboro (BRAT) rats (see Valtin, 1982) have reported deficits in cognitive functioning and learning. For example,

*Correspondence to: Psychology Department, Northern Michigan University, Gries Hall, Room 306, 1401 Presque Isle Avenue, Marquette, MI 49855, USA. Fax: +1 906 227 2954.
E-mail address: aprus@nmu.edu (A.J. Prus).

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BRAT rats exhibit attenuated conditioned freezing responses (Stoehr et al., 1993), display delayed acquisition and maintenance of passive avoidance behavior (Bohus et al., 1975; De Wied et al., 1975; although see Williams et al., 1983 and Brito et al., 1982), display an impaired ability to retain spatial information in a delayed alternation task (measured in rats carrying the Brattleboro diabetes insipidus gene; Colombo et al., 1992; although see Brito et al., 1982), demonstrate deficits in prepulse inhibition (e.g., Feifel and Priebe, 2001; Feifel et al., 2010; Cilia et al., 2010), and display deficits in social discrimination (Feifel et al., 2009). However, deficits have not been reported between BRAT rats and Long–Evans (LE) rats, which serve as the wild type strain for BRAT rats in a delayed alternation t-maze task or a visual and olfactory discrimination task (Brito et al., 1982), and have been reported to require fewer sessions to learn a positively reinforced operant conditioning task (Laycock et al., 1983).

While a number of studies have examined learning, conditioning, and memory in vasopressin-deficient rats, only two studies have specifically examined attention in vasopressin deficient rats, which were conducted using a lateralized reaction time task (Jentsch et al., 2003; Jentsch, 2003). This task required rats to emit a nose poke when a signal light was presented into one of two apertures that were positioned on either side of a central aperture. Behavior in this task consisted of a rat emitting nose pokes into the central aperture until a signal occurred, and task difficulty was adjusted by changing the duration of time between signals, and accurate performance relies on both sustained and divided attention. In this task, BRAT rats displayed both impairments and improvements in attention, depending on the duration of time before a signal was presented (Jentsch et al., 2003), while HZ rats displayed improvements in attention at short durations but no effects at longer durations (Jentsch, 2003). Thus, this previous research illustrates a complex picture of the role for vasopressin in attention processes, which may be clarified upon testing vasopressin-deficient animals in other attention tasks.

A common method for assessing attention is the five-choice serial reaction time task (5-CSRTT; for review, see Robbins, 2002). Unlike the lateralized reaction time task, the 5-CSRTT requires animals to attend to a stimulus light presented randomly in one of five apertures. Each trial in a 5-CSRTT begins several seconds after an animal accesses the chamber's food receptacle. This task is regarded as an assessment of attention accuracy, including spatial attention, divided attention, attention shifting, and inhibitory control (for review, see Amitai and Markou, 2010; Chudasama and Robbins, 2004; Robbins, 2002).

The present study sought to assess attention in vasopressin deficient rats by studying male and female BRAT, HZ, and LE rats in a modified, self-paced version of the 5-CSRTT. Unlike the traditional 5-CSRTT, the present study required a rat to press a lever to initiate each trial. This preparatory response was intended to control for possible differences in motivation, ambulation, or other factors (Williams et al., 1983; Schank, 2009; Cilia et al., 2010) that might be different between these strains. Animals were trained until they attained a stable level of accuracy, and then these levels were compared between strains.

2. Results

2.1. Experiment one: assessment of attention in male rats

2.1.1. Number of sessions to complete all training phases in the male rats

Rats were determined to have failed to learn the task if they exceeded the number of sessions to meet a training phase by over two standard deviations, compared to the mean number of sessions needed by the other rats of the same strain and sex. The number of male rats completing the final phase of training criteria consisted of the following: LE rats (6 out of 9 rats; 1 male rat died during the training period); HZ rats (9/10); and BRAT rats (6/10). A chi square analysis failed to reveal statistically significant differences between strains for the number of rats that completed the training (data not shown).

Fig. 1a presents the mean number of sessions to meet criteria for the male rats. Statistically significant effects were found between strains in males, $F(2,18)=4.022$, $p<0.05$, which were due to BRAT rats requiring more sessions to meet the training criteria than those of LE and HZ rats.

2.1.2. Percent accuracy

Percent accuracy did not differ significantly between strains (Fig. 1b).

2.1.3. Percent premature responses

No statistically significant effects were found in premature responses between strains (Fig. 1c).

2.1.4. Percent omissions

No statistically significant effects were found for omissions between strains (Fig. 1d).

2.2. Experiment two: assessment of attention in the female rats

2.2.1. Number of sessions to complete all training phases

The number of rats completing the final phase of training criteria consisted of the following: LE (9 out of 10 rats); HZ (6/10); and BRAT (5/8). A chi square analysis revealed no statistically significant differences between strains for the number of rats that completed training (data not shown). No statistically significant differences were found in the mean number of sessions to meet criteria for the female rats (Fig. 2a).

2.2.2. Percent accuracy

A statistically significant effect was found between stains in female rats, $F(2,17)=4.330$, $p<0.05$, which were due to female rats exhibiting significantly lower percent accuracy compared to HZ and LE rats (Fig. 2b).

2.2.3. Percent premature responses

No statistically significant effects were found in premature responses between strains (Fig. 2c).