Puberty dependence of (AVP) expression in the BNST and MeA (Social Behavior Circuit)

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INTRODUCTION

Social development is critical for an individual's overall health and wellbeing. Apart from reproductive competence, adolescents undergo social, emotional, cognitive and physical development (Spear, 2000). One such neurotransmitter that governs social behavior is Vasopressin (Arginine Vasopressin or AVP).

So far, it was indicated that pubertal factors underlie social behavior development. This study investigates the development of the social behavior circuit: onset of Vasopressinergic projections in the Bed Nucleus Stria Terminalis (BNST) and the Medial Amygdala (MeA). It questions the gonadal steroid influence on the pathway development (puberty dependent) and highlights the onset of vasopressin expression that develops independently of the hypothalamic-pituitary-gondal (HPG) axis activation (puberty-independent).

This remarkable discovery initiates one's thought processes towards other behavioral patterns governed by AVP, specifically mating behaviors. Further research into the developmental onset of the social behavior circuit in juveniles is necessary to derive neural correlates for mating styles (monogamous and polygamous).

Keywords: social development, vasopressin, mating styles, monogamous, polygamous

SOCIAL BEHAVIOR & ITS DISSOCIATION FROM PUBERTY

Uncovering the mechanisms that contribute to behavioral research often incorporates the use of animal models such as rodents, as they provide molecular similarity with humans and mimic numerous diseases found within us (Smith, Bolton, & Dwinell, 2019).

Social play is an ideal behavior to study social development in animals. It is an evolutionarily conserved behavior exhibited in most mammals (Bekoff, 1984; Eisenberg, 1981). Play behavior emerges during the juvenile stage in rats and hamsters around postnatal day (P)18, peaks during early to mid-adolescence (~P35), and then declines thereafter (Panksepp, 1981). Play behavior can be assessed by documenting frequencies and durations of behaviors such as attacks and pins (Paul, Probst, Brown, & de Vries, 2018).

Puberty, characterized by the activation of the reproductive axis (HPG), can be manipulated by either gonadectomy or the seasonal approach. Photoperiod-dependent neural circuits of Siberian hamsters can be manipulated by altering the light/dark cycles. For example, a 20-hour exposure to light implies a Long Day (LD) cycle, indicative of summer, while a 15-hour exposure to light implies a Short Day (SD) cycle, indicative of winter. Such photoperiodic manipulations cause several seasonal adaptations in fur, body weight, testes size and vaginal opening. A dissociation from puberty was successfully obtained in SD-reared male and female hamsters, wherein delays in Estimated Testicular Volume (ETV) and Percentage of Vaginal Opening, respectively were recorded ((Paul et al., 2018), Fig.1). Furthermore, puberty-independent regulation of play and aggressive behaviors were also observed ((Paul et al., 2018), Fig.1).

The neural mechanisms regulating play behavior are yet to be understood. Studies indicate the involvement of arginine vasopressin (AVP) (Cheng, Taravosh-Lahn, & Delville, 2008).

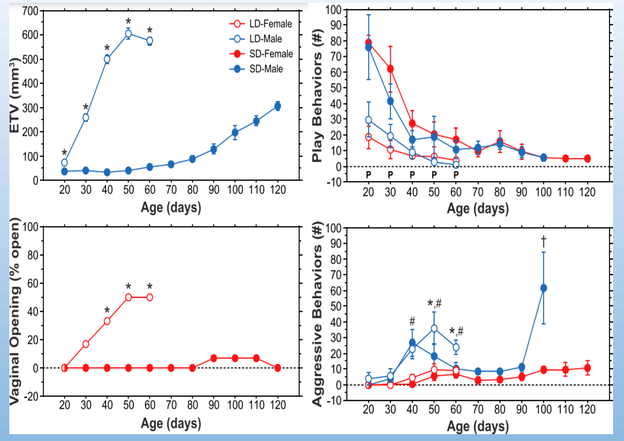

Fig. 1. Photoperiod-dependent dissociation from puberty and puberty-independent social behaviors exhibited by Siberian Hamsters (Paul et al., 2018).

VASOPRESSIN AND SOCIAL BEHAVIOR

Male and female juvenile Brattleboro rats, lack AVP throughout development due to a mutation in the AVP gene (Schmale et al., 1993).

The impact of AVP on play behavior can depend on sex of the subject, brain region manipulated, and type of manipulations (acute pharmacological manipulation vs. chronic genetic mutation). Brattleboro rats exhibit an atypical social behavior profile characterized by decreased social play behaviors and an increase in huddling compared to their wild-type counterparts that have normal vasopressin production and secretion ((Paul et al., 2016); Fig. 2). While these experiments indicate a role for vasopressin in juvenile social behavior, they cannot determine the pathway by which AVP exerts its effects.

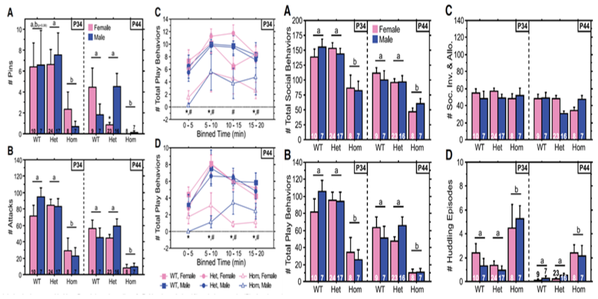

Fig. 2. Social behaviors and Play behaviors exhibited by Brattleboro rats in comparison to those seen in Het and WT. (Paul et al., 2016).

VASOPRESSIN PATHWAYS

AVP employs several pathways to regulate behavioral and physiological functions including circadian rhythms, water balance, stress, autonomic function and social behavior. The sexually dimorphic parvocellular VP projections from the BNST and the MeA, projecting towards the LC, LH, LS and VSA, are involved in depicting social behaviors ((de Vries & Miller, 1998); Fig. 3).

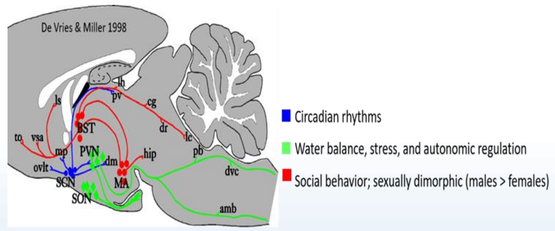

Fig. 3. Vasopressin pathways (de Vries & Miller, 1998). Known for its involvement in displaying social behaviors, steroid-sensitive, sexually dimorphic projections from the bed nucleus of stria terminalis (BNST) and medial amygdala (MA) project towards the olfactory tubercle (to), lateral septum (ls), lh, central grey (cg), dorsal raphae nucleus (dr), locus coeruleus (lc) and the hippocampus (hip). Circadian circuit originates in parvocellular cells in the suprachiasmatic nucleus of the hypothalamus (SCN), with projections extending toward the paraventricular nucleus of the hypothalamus (PVN), medial preoptic area (mp), organum vasculosum of the lamina terminalis (ovlt) and the lateral habenula (lh). Furthermore, the water balance circuit, stemming from the SCN, SON and PVN, project toward the MA, dorsal vagal complex (dvc) and nucleus ambiguous (amb).

ONTOGENY OF VASOPRESSIN PROJECTIONS IN LS & LH

Studies indicate that AVP pathways develop from the BNST and MeA, and project outward to the lateral septum (LS) and lateral habenula (LH) regions. Upon analyzing AVP fiber development in the LS, a sexually dimorphic pattern was recorded, indicating a denser in fiber network in males (right) than in females (left) (Panzica & De Vries 2006).

Rats are said to be in adolescence between postnatal (P) 35 and 63 days (Sengupta, 2013). AVP Fiber development in the LS and LH for males begins at P12 and peaks at P14, and in females, doesn't begin till P55 or even until adulthood ((de Vries, Buijs, & Swaab, 1981); Fig. 4).

Data analyzed does indicate the sexually dimorphic nature of the ontongeny of vasopressinergic projections.

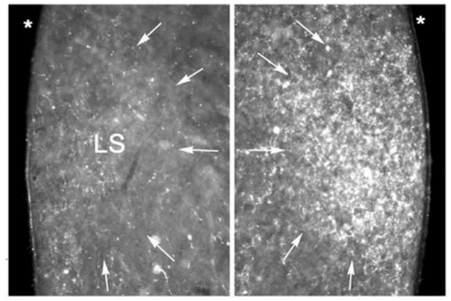

Fig. 4. Males (right) show denser AVP fiber development than females (left) in the lateral septum (LS) (Panzica & De Vries 2006).

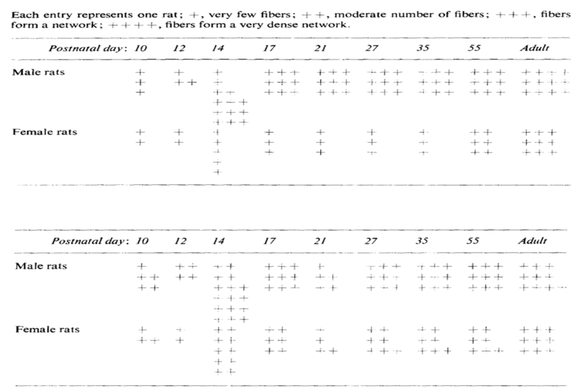

Fig. 5. Density of AVP fibers in the lateral septum (above) and lateral habenula (below) during development (de Vries, Buijs, & Swaab, 1981).

GONADAL-STEROID INFLUENCE ON AVP EXPRESSION

Sexual dimorphism was also observed in the Bed Nucleus Stria Terminalis (BNST) and the Medial Amygdala (MeA) when analyzing the number of cells expressing Vasopressin: density of AVP-labelled cells was higher in males than in females ((De Vries 1994); Fig. 6). Upon gonadal-steroid influence however, the number of AVP-expressed cells spiked in the presence of Estradiol (E) and a combination of Estradiol and Dihydrotestosterone (E+DHT), with no observable change recorded in the presence of just (DHT). Furthermore, in males, there was a higher spike in expression of AVP-labelled cells in the presence of (E+DHT) when in comparison with rise recorded in the presence of (E) ((De Vries 1994); Fig. 6).

Thus, one can concur that the gonadal steroid hormonal levels during puberty, impacts AVP fiber development in the BNST and MeA (Social behavior pathway).

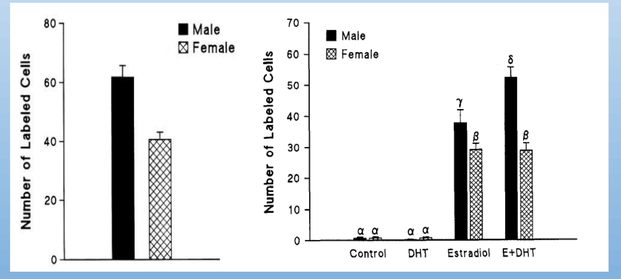

Fig. 6. The development of the Bed Nucleus Stria Terminalis (BNST) and Medial Amygdala (MeA) associated social behavior pathway might be triggered by increased gonadal steroid hormone levels during puberty (De Vries 1994).

DISCUSSION

Although, AVP-expression shows dependence on gonadal-steroid manipulations, it does not explain the onset of AVP-fiber development. In fact, in the social behavior circuit, AVP-fiber development in the LS and the LH has already been documented at P12 in males, which is indicative of juvenile stages, not adolescence ((de Vries, Buijs, & Swaab, 1981); Fig. 5). Thus, one can also speculate that the vasopressinergic pathway develops prior to puberty.

There definitely exists an argument regarding the pubertal influence on AVP expression, however several non-pubertal mechanisms could govern the ontogeny of the social behavioral circuit. Further research is necessary to draw upon a conclusion regarding the pubertal dependence of the AVP pathway development.

AVP has been implicated in several neurodevelopmental disorders such as ASD, ADHD, and Schizophrenia (Bilgiç, Toker, & Uysal, 2016; Francis et al., 2016). Vasopressin-dependent social behavior and attachment pathways in the brain indicate that one's mating style correlates with the density of the type of vasopressin receptor expressed in the hypothalamus, i.e., AVPR1a/V1AR for monogamous behaviors (Ren, Chin, & French, 2014). Further analysis of the social behavior circuit would help establish neural pathways govering mating styles and their developmental onset in juvenile stages.

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