

Posters**P.2.001 Measuring motivation and performance of social play behavior in rats: role of dopamine and noradrenaline**

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Social play behavior is a vigorous form of social interaction, abundant in the young of many mammalian species, including humans. The experience of social play behavior during childhood and adolescence is critical for normal social and cognitive development. In rats, social play is characterized by distinct behaviors, (1) pouncing (invitation to play), when one animal attempts to touch the nape of the neck of another animal and (2) pinning (continuation play bout), upon contact of the nape, the recipient animal fully rotates around the longitudinal axis of its body, ending in a supine position with the other animals standing over it. Social play is highly rewarding, and as such, the expression of social play depends on its pleasurable and motivational properties [1–3]. Because dopamine and noradrenaline have been implicated in both social play and in reward processes, we here investigated the role of dopamine and noradrenaline in the pleasurable and motivational properties of social play behavior in rats. To assess social play motivation, we developed a setup in which rats responded for access to a playful partner under a progressive ratio schedule of reinforcement. To assess the pleasurable properties of social play, the acquisition of social play-induced conditioned place preference (CPP) was investigated. The psychostimulant drugs methylphenidate and cocaine both increased responding for social play (measured by the number of rewards obtained and the breakpoint reached), suppressed its expression (measured by the frequency of pinning and pouncing) but did not affect its pleasurable properties (measured by the time spent in the play associated compartment compared to the non-play compartment). The noradrenaline reuptake inhibitor atomoxetine decreased both social play motivation and expression, but spared social play-induced place conditioning. The dopamine reuptake inhibitor GBR12909 increased motivation for social play, did not affect its expression, but reduced its pleasurable properties. The effect of methylphenidate and cocaine on social play motivation was blocked by

the dopamine receptor antagonist α -flupenthixol whereas play expression remained suppressed. Furthermore, the α -2 adrenoceptor antagonist RX821002 reversed the play-suppressing effect of methylphenidate, but left its effect on motivation for social play unaltered. The doses used of both the dopamine receptor antagonist α -flupenthixol and the α -2 adrenoceptor antagonist RX821002 did not affect operant responding or play behavior. These data demonstrate dissociable roles for dopamine and noradrenaline in social play behavior: dopamine is involved in the motivational and pleasurable properties of social play, whereas noradrenaline modulates the motivation for play and its expression. These data provide new insights into the intricate mechanisms by which catecholamines modulate social play behavior in rats. Elucidating the neural underpinnings of social behavior in the young may increase our understanding of normal, adaptive social development, and may shed light on the pathophysiology of childhood and adolescent psychiatric disorders characterized by aberrant social behavior such as autism spectrum disorder (ASD) or attention deficit/hyperactivity disorder (ADHD).

Reference(s)

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P.2.002 Ultrasonic vocalization and homing behavior in the valproic acid rat model of autism spectrum disorders: role of the endocannabinoid system

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Purpose of the study: Autism spectrum disorders (ASD) are a range of complex neurodevelopment disorders, characterized by impaired social behavior and communication and repetitive patterns of behavior. No effective treatments are yet available for ASD, and preclinical models that mimic the main symptoms of the disease are essential to find potential pharmacological targets. Prenatal exposure to valproic acid (VPA) has

been proposed as a rodent model of autism spectrum disorder. Given the altered social communication found in autistic children since early development, the first purpose of this study was to investigate whether VPA prenatal exposure alters ultrasonic vocalization (USV) emission and homing behavior in the rat offspring. Furthermore, since several studies have revealed the involvement of the endocannabinoid system in the regulation of social and emotional behavior, the second purpose of this study was to test the ability of cannabinoid drugs to correct behavioral deficits found in VPA-exposed rats.

Methods: Female Wistar pregnant rats received an intraperitoneal (i.p.) injection of either VPA (500 mg/kg/250 ml) [1], or the same volume of saline solution (VEH) at gestational day 12. After delivery, at post natal day (PND) 5, 9 and 13 each pup was separated from the nest for 3 minutes, during which the shape and the frequency of USVs were studied using the Software AvisoftSASLab. At PND 13 the offspring was tested in the homing test: each pup was placed individually in a small box with base covered by sawdust for 4 minutes. The time spent by the pups to reach the sawdust of their own litter and the time they spent in each side of the box were evaluated. In the second part of the study, we tested the effects of URB597 (0.025 mg/kg/2.5 ml), that inhibits the hydrolysis of the endocannabinoid anandamide, in rats prenatally exposed to either VPA or vehicle.

Results: The analysis of USV emission revealed that VPA-prenatally exposed male animals vocalized less compared to VEH-exposed males at PND 5 ($p < 0.05$) and at PND 9 ($p < 0.05$). In the homing test, the VPA-prenatally exposed male animals showed a decrease in the latency to reach their litter box ($p < 0.05$) and in the time spent in the litter box ($p < 0.05$) compared to VEH-exposed male animals. No differences in USV emission and homing behavior were found between female rats prenatally exposed to either VPA or VEH. Ongoing experiments are evaluating the effects of URB597 in the USV and homing tests in VPA- and VEH-exposed offspring.

Conclusion: Altogether, these findings reveal socio-emotional and cognitive alterations in male rats prenatally exposed to VPA and tested during infancy. Thus, early embryonic exposure to VPA in rats provides a good model for several specific aspects of ASD and is a valuable tool to explore pathophysiological hypotheses and to evaluate potential treatments.

Reference(s)

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