Review

The pleasures of play: pharmacological insights into social reward mechanisms

Viviana Trezza[1,3], Petra J.J. Baarendse[1] and Louk J.M.J. Vanderschuren[1,2]

[1] Department of Neuroscience and Pharmacology, Rudolf Magnus Institute of Neuroscience, University Medical Center Utrecht, Utrecht, The Netherlands
[2] Department of Animals in Science and Society, Division of Behavioural Neuroscience, Faculty of Veterinary Medicine, Utrecht University, Utrecht, The Netherlands
[3] Department of Biology, University 'Roma Tre', Rome, Italy

Like human children, most young mammals devote a significant amount of time and energy playing together, and social play is fun. Although social play is very pleasurable, it is more than just a frivolous activity: it is crucial for the development of behavioral flexibility, the acquisition of social and cognitive competence, and the maintenance of group cohesion. Social play is a natural reinforcer, and the neurotransmitter systems intimately implicated in the motivational, pleasurable and cognitive aspects of natural and drug rewards, such as opioids, endocannabinoids, dopamine and norepinephrine, play an important modulatory role in the performance of social play. In this review, we address the notion that social play is rewarding, and discuss recent developments in the neuropharmacology of this behavior. This provides a framework to understand how the brain processes social emotions, to make young individuals enjoy social play.

Introduction

Social behaviors, such as affiliative, sexual, parental and aggressive territorial behaviors, are an integral part of the mammalian behavioral repertoire essential for survival of the individual, group or species. Social play behavior, also referred to as 'rough and tumble play', is the earliest form of mammalian social behavior that is not directed at the mother, but at peers [1–3]. Similar to human children, most young mammals spend a substantial part of maturation engaging in play with peers, such as running, chasing, climbing and play fighting. The ability to engage in social play is one of the principal indicators of healthy development, both in animals and humans. Conversely, social play deficits are a core symptom of neuropsychiatric disorders in childhood and adolescence, such as autism, early-onset schizophrenia, and attention-deficit/hyperactivity disorder (ADHD) [4–6].

'Playing' and 'having fun' are almost synonymous. Indeed, perhaps the most prominent characteristic of social play is its high reward value [1–3]. However, although there seems to be no obvious direct function of play other than having fun, social play does have clear benefits. By varying, repeating, and/or recombining subsequences of behavior outside their primary context, play serves to develop physical, cognitive and social capacities, and especially to acquire the ability to flexibly use these capacities under changeable circumstances [3,7]. More specifically, play experience in a social context is crucial for the development of normal socioaffective responses and the acquisition of social skills [8,9]. Social play might also serve to facilitate the development of other, non-social, cognitive capacities. Besides these developmental functions, social play has stress-reducing effects, and serves to maintain group cohesion [3]. These latter properties, as well as maintenance of the skills previously acquired through play, are probably the functions of social play behavior in adult animals [3].

Social play is characterized by its vigorous appearance, exaggerated forms of behavior, and high level of affiliation. The most detailed and extensive experimental research investigating mammalian social play has been performed in the laboratory rat (*Rattus norvegicus*) [1–3,10]. As in almost every mammalian species studied, rats engage in social play according to an inverted U-shaped curve in ontogeny, peaking during the juvenile period and then falling off around puberty [1–3]. Patterns of adult affiliative, sexual and aggressive behavior can be recognized in social play, although young and adult social behavior differ in intensity, form and contextual settings [2,3]. In rats, a bout of social play behavior starts with one rat soliciting (pouncing) another animal, by attempting to nose or rub the nape of its neck (Figure 1a). The animal that is pounced upon can respond in different ways: if the animal fully rotates to its dorsal surface, 'pinning' is the result (Figure 1b). Pinning is regarded as the most characteristic posture in social play in rats. As rats mature into adulthood, the structure of social play changes. Most prominently, the response to pouncing with full rotation to the dorsal surface (resulting in pinning) occurs less, and is replaced by evasions and partial rotations [3] (see Table 1 for a detailed description of the different components of social play behavior in rats).

Just like other naturally rewarded behaviors that are important for development and survival, such as feeding, drinking, and sexual behavior, social play is a reinforcer

Corresponding authors: Trezza, V. (vtrezza@uniroma3.it); Vanderschuren, L.J.M.J. (l.j.m.j.vanderschuren@umcutrecht.nl).

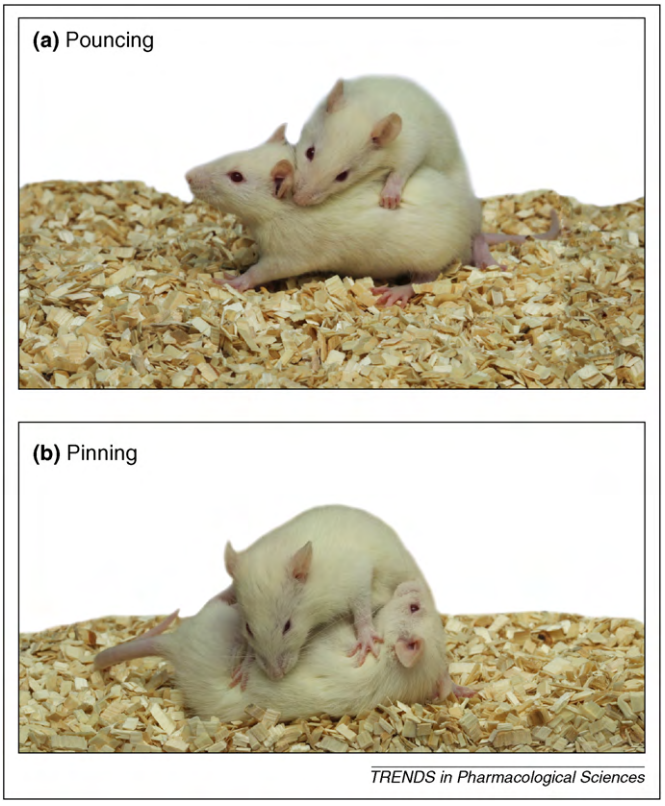

Figure 1. The most characteristic postures of social play in young rats. **(a)** Pouncing; **(b)** pinning. For a detailed description of the different components of social play behavior in rats, see Table 1.

both in rats and non-human primates [11–22]. Research into the neurobiological underpinnings of social play behavior has provided a substantial body of evidence that it is modulated by the neural systems that also mediate the positive subjective and motivational properties of food, sex and drugs of abuse. In this review, we provide an overview of recent advances in the neuropharmacology of social play behavior. We will restrict ourselves to studies in rats, because the vast majority of pharmacological studies on social play behavior has been performed in this species (see [23,24] for examples of pharmacological studies in hamsters and monkeys). We focus on opioids, cannabinoids, dopamine and norepinephrine, the neurotransmitter systems that modulate the rewarding, motivational and cognitive aspects of this behavior (Table 2). Comprehensive overviews of pharmacological studies on social play, addressing the role of other neurotransmitters, such as gamma aminobutyric acid (GABA), acetylcholine and adenosine, can be found in previous reviews [2,10].

Rewarding properties of social play

The earliest demonstrations of social reinforcement came from studies in primates, which showed that a chimpanzee learned a discrimination task that was rewarded by the opportunity to groom the experimenter [21]. The reinforcing properties of social play were subsequently shown by Mason *et al*. [22]. In this study, chimpanzees had the choice of pressing one of two levers. Pressing one lever produced food, and pressing the other lever produced social interaction. The experimenters manipulated the incentive value of the food reward by testing the animals when hungry or sated, or by offering foods of different palatability. The social interaction on offer was either petting or play. Food was chosen more often when the animals were hungry and when the most preferred food was available. Of the social behaviors, play was more reinforcing than petting. Intriguingly, even when the animals were tested hungry, they chose play on almost half of the occasions. When tested sated and offered foods of different palatability, the animals still chose play on half the occasions, even when the food reinforcer was very palatable. This pioneering study showed that social play is a powerful reinforcer in chimpanzees, comparable on a reward basis with tasty food. Rewarding properties of social play behavior in rats have since been demonstrated using both T-maze discrimination tasks [11,16,17] and place conditioning [12–15,18–20]. Rats will readily learn a T-maze discrimination task when rewarded with a social interaction, most prominently social play. Indeed, interactions with a partner that has been rendered non-playful (but not non-social) by physical confinement or drug treatment are less rewarding than playful social interactions [11]. It has repeatedly been shown that social play behavior can induce conditioned place preference [12–15,18–20]. Place conditioning studies have provided further evidence that it is indeed social play, rather than social interaction in general, that is rewarding, because interactions with non-playful animals did not induce conditioned place preference [12,15]. In addition, it has been shown that the positive subjective properties of cocaine or nicotine and social play can act synergistically, even if social play is reduced by these drugs [13,14]. Another line of empirical evidence to support the notion that social play is rewarding comes from studies showing that during social play, rats emit high frequency (~50 kHz) vocalizations [25] that are also emitted during other pleasurable events, such as sexual behavior and drug-induced conditioned place preference. Together, these data indicate that social play is rewarding, in the sense that it can be used as an incentive for maze learning, lever pressing and

Table 1. Ethogram of the social repertoire of young rats.

Behavior	Description
Pouncing	Nuzzling the nape of the conspecific's neck with the tip of the snout, followed by a rubbing movement (Figure 1a)
Evasion	Upon solicitation, the recipient animal avoids contact with the nape by leaping, running, or turning away from the partner
Partial rotation	Upon contact of the nape, the recipient animal begins to rotate along its longitudinal axis, but then stops and keeps one or both hind feet firmly planted on the ground
Pinning	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 subject standing over it (Figure 1b)
Boxing/wrestling	Rearing in an upright position towards the other subject, combined with both rats rapidly pushing, pawing, and grabbing at each other, or one rat wrapping around the other subject.
Following/Chasing	Moving or running forward in the direction of or pursuing the other subject, who moves away
Social exploration	Sniffing, licking or grooming any part of the body of the test partner, including the anogenital area