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Domestication and the Role of Social Play on the Development of Sociocognitive Skills in Rats

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Several studies on rats and hamsters, across multiple laboratories, have shown that limiting play in the juvenile period leads to adults that have physiological and anatomical changes in the medial prefrontal cortex (mPFC) and reduced sociocognitive skills. Peers raised with playful peers have better sociocognitive skills than animals raised with adult partners. Using Long Evans hooded rats - a commonly used domesticated strain - this relationship has been replicated multiple times. However, when the same paradigm was used with laboratory-reared wild rats, no differences were found between rats reared with peers and ones reared with adults. It has been shown that the key play-generated experiences involved are those related to actively wrestling with a partner and turn taking (as measured by role reversals), which give both partners opportunity to gain the advantage during play fighting. In the present study, we tested the hypothesis that wild rat adults provide juveniles more such experiences than do adult Long Evans rats. The asymmetry in the play interactions in adult-juvenile pairs was compared between the two strains. As predicted, wild rat adults initiated more play with the juveniles, wrestled more, and provided more opportunities for role reversals. The findings thus support the hypothesis for the observed strain differences in the effects of rearing condition on the mPFC.

Keywords: play fighting, rats, medial prefrontal cortex, reciprocity, brain plasticity, domestication

When rats are reared in social isolation over the juvenile period (i.e., from weaning to sexual maturity), they exhibit, as adults, a range of neural, behavioral, emotional and cognitive deficits (e.g., Arakawa, 2002, 2003; Byrd & Briner, 1999; da Silva, Ferreira, Carobrez, & Morato, 1996; Einon & Potegal, 1991; Fone & Porkess, 2008; Hall, 1998; Potegal & Einon, 1989; van den Berg et al., 1999). Rearing regimes in which the animals have some degree of access to social partners, but with that access providing little to no opportunity to engage in social play, still lead to adults with sociocognitive deficits, indicating that at least part of the effects of social isolation is due to failure to gain the experiences derived from playing with peers in the juvenile period (e.g., Baarendse, Counotte, O'Donnell, & Vanderschuren, 2013; Einon, Morgan, & Kibbler, 1978; Pellis, Field & Whishaw, 1999; Schneider, Pätz, Spanagel, & Schneider, 2016; Schneider et al., 2014; Schneider, Bindila, et al., 2016; van Kerkhof, Damsteegt, Trezza, Voorn, & Vanderschuren, 2013). It has been hypothesized that social play affects the development of the medial prefrontal cortex (mPFC) and associated sociocognitive skills by providing experiences that require the rats to engage those skills during play (Pellis, Pellis, & Himmler, 2014; Vanderschuren & Trezza, 2014).

Social play in rats is mostly in the form of play fighting, which involves attack and defense of the nape of the neck, which, if contacted, is usually gently rubbed with the snout (Pellis & Pellis, 1987; Siviy & Panksepp, 1987). While play fighting may superficially resemble serious fighting, it differs, in that for such play to remain playful and not escalate to serious fighting, there has to be some degree of reciprocity with both partners taking turns in gaining the advantage (Altmann, 1962). How turn-taking is achieved and the degree of turn-taking can vary with species, age, and sex (for a review of the literature on this issue, see Pellis & Pellis,

2017). In rats, such reciprocity involves relaxing the vigor of defensive actions and partners, in an advantageous position, compromising their own ability to mitigate counterattacks from a partner (Pellis & Pellis, 1998; Pellis, Pellis, & Foroud, 2005). This reciprocity, which is facilitated by modifications of attack and defense, is most exaggerated during the peak period of play in the juvenile phase (Foroud & Pellis, 2002, 2003) between 30-40 days after birth (Thor & Holloway, 1984). At this age, about 30% of play fights that are initiated by one partner result in a role reversal, in which the original attacker becomes the defender (Himmler, Himmler, Pellis, & Pellis, 2016). Tracking of wins and losses, attending to the actions of one's partner and of oneself, then adjusting actions appropriately to maintain a suitable degree of reciprocity likely engage the sociocognitive skills that involve the mPFC and, by doing so, train those mechanisms (Pellis et al., 2014). Two lines of research strongly implicate these reciprocal exchanges as key for altering the mPFC and training sociocognitive skills.

First, rearing Long Evans hooded rats (LE) over the juvenile period with an adult leads to their developing an anatomically altered mPFC compared to the mPFC of juveniles which are reared with same age peers (Bell, Pellis, & Kolb, 2010; Himmler, Pellis, & Kolb, 2013), and detailed analyses of the play that occurs in adult-juvenile pairs reveal that juveniles experience fewer opportunities for reciprocal exchanges (Pellis, Williams, & Pellis, 2017). Second, when Wistar rats, a highly playful strain (Himmler, Modlinska, et al., 2014), are reared with Fischer 344 peers, a less playful strain (Siviy, Baliko, & Bowers, 1997; Siviy, Love, DeCicco, Giordano, & Seifert, 2003), they not only experience fewer reciprocal exchanges than when reared with Wistar peers, but they also exhibit reduced sociocognitive skills later in life relative to Wistars reared with Wistars (Schneider, Bindila, et al., 2016; Schneider, Pätz, et al., 2016). It should be noted that in both of these lines of research, females were used, which is the reason that the current study also focused on females (see **Method**).

In the brains of LE rats, the mPFC undergoes more dendritic pruning when the rats are reared with peers compared to when they are reared with an adult – a finding that we have replicated numerous times (Bell et al., 2010; Himmler, Pellis, & Kolb, 2013; Himmler et al., 2018). In a study using the same paradigm, greater pruning and improved sociocognitive skills were shown to occur in another species of laboratory rodents, the Syrian golden hamster (Burleson et al., 2016), suggesting that such an effect of play is not limited to rats. However, using the same paradigm that we used with LE rats with laboratory-housed wild rats, the Warsaw Wild Captive Pisula Stryjek strain (WWCPS) did not show such an association. Rather, whether reared with a peer or an adult, the degree of dendritic pruning in the mPFC was the same (Himmler, 2015; Pellis, Himmler, Himmler, & Pellis, 2018). One possibility is that the play/mPFC/sociocognitive-skill association is an artifact of domestication – that is, it is a byproduct of the broad range of anatomical, physiological, and behavioral changes produced by the domestication process (Wilkins, Wrangham, & Fitch, 2014). Somehow, the mPFC may be more plastic in domesticated laboratory rats and so more sensitive to the effects of play-generated experiences (Pellis et al., 2018). However, a recent study of Belding's ground squirrels showed that those that engaged in more social play as juveniles had greater sociocognitive skills as adults (Marks, Vizconde, Gibson, Rodriguez, & Nunes, 2017). Given that this study extends the association between juvenile play and the development of sociocognitive skills to a nondomesticated species of rodent, this lessens the likelihood that the association present in laboratory rats and hamsters is an artifact of increased brain plasticity due to domestication. This raises an alternative possibility: Under conditions of domestication, adults are less likely to play with juveniles and so are less likely to generate the experiences derived from turn-taking that are critical for the developmental refinement of the mPFC.

Experimental handling of rat pups in the first two weeks of postnatal life induces developmental changes in hippocampus function and the stress response system (Levine, Lyons, & Schatzberg, 1997). These manipulations involve separating the infant from its mother for a short period of time during which the infants

emit ultrasonic distress calls. In turn, these calls elicit increased maternal care, such as licking, when the infant is returned to its home cage (Liu et al., 1997). It has been suggested that, in laboratory conditions in which water and food are freely available, humidity and temperature are invariant, and there are no predators, some mothers do not care for their young as well as they would under more naturalistic conditions (Bateson & Martin, 2000), an effect that may be exacerbated by domestication. Similarly, the reduced interest of laboratory rat mothers and other adults in interacting playfully with juveniles (Pellis & Pellis, 1997; Pellis et al., 2017; Pellis et al., 2018) may be a byproduct of domestication coupled with the relatively invariant and unstimulating laboratory environments. Being reared alone in the absence of peers with a wild mother in the third to fourth week after birth, the age at which play emerges and matures to its juvenile-typical form (Baenninger, 1967; Bolles & Woods, 1964; Pellis & Pellis, 1997), leads to the development of play fighting that is indistinguishable from that of rats reared with littermates (Himmler et al., 2015). These findings suggest that wild adult female rats, unlike their domesticated counterparts, may provide more of the play experiences needed by juveniles than that provided by domesticated mothers. If this hypothesis is correct, then, in wild rats, the juveniles may gain sufficient experiences in turn-taking when playing with an adult that are only provided by peers in domestic rats. This could account for the difference in the play-induced changes to the mPFC between domestic LE rats and wild rats (Himmler, 2015; Pellis et al., 2018). The present paper tests this hypothesis by comparing the play of adult-juvenile pairs of LE rats and WWCPS rats.

Juvenile WWCPS rats, like the juveniles from domestic strains, mostly attack and defend the nape of the neck, but they initiate less playful attacks than do domestic strains and, compared to LE rats in particular, are more likely to use evasive defensive actions to defend the nape than to wrestle with the partner to do so (Himmler, Modlinska, et al., 2014; Himmler, Stryjek, et al., 2013). Adult LE rats are less likely to initiate playful attacks with juveniles than juveniles are with other juveniles, are less likely to defend against attacks by juveniles, and, when they do so, are more likely to evade than wrestle (Pellis et al., 2017). Casual observation suggests that adult wild rats are similarly less predisposed to play with juveniles (Pellis et al., 2018). From these observations, we propose several predictions about the play behavior of adult-juvenile pairs: (1) WWCPS pairs should initiate fewer play fights than LE pairs, (2) in both strains, the juveniles should launch more nape attacks than their adult partners, (3) the adults of both strains should be equally likely to defend against attacks by juveniles, and (4) when the adults do defend themselves, both strains should be equally likely to do so by evading. That is, there should be a strain difference in the amount of play, and adults of both strains should be equally reluctant to play with juveniles. However, for the hypothesis to be supported, the relative asymmetry between adults and juveniles should be less in the WWCPS rats than in the LE rats, especially with regard to aspects of play fighting related to reciprocity. Consequently, if the hypothesis is correct, we make the following additional predictions: (5) While in both WWCPS and LE rats the juvenile should initiate the majority of the play fights, the relative proportion initiated by the adult should be greater in the WWCPS rats, (6) a greater proportion of interactions involving WWCPS adults should lead to active wrestling competitions with mutual attempts to gain access to each other's napes, (7) a greater proportion of play fights involving wild adults should lead to role reversals, and (8), most critically, a greater proportion of role reversals in the wild rats should be initiated by the juvenile partner.

Method

Subjects

As both the effects of rearing on the development of the mPFC (Bell et al., 2010; Himmler, 2015; Himmler et al., 2013) and the behavioral analyses of the play experiences in those rearing environments (Pellis, Williams, & Pellis, 2017) involved females, the present study used females. A total of 28 female rats were used. Twelve subjects were LE rats obtained from Charles River Laboratories (St. Constant, Quebec) and maintained in the animal facility at the Canadian Centre for Behavioral Neuroscience (University of Lethbridge). They were kept in 46 cm × 25 cm × 20 cm polyethylene tubs with processed corncob bedding at a constant 21-23°C on a 12:12-hr light-dark cycle with lights off at 19:30. Food and water were provided ad libitum. All animals were handled and cared for in accordance with the Canadian Council for Animal Care regulations, with the experimental use of the animals being approved by the animal care committee of the University of Lethbridge.

The remaining 16 rats that were used were WWCPS rats derived in 2006 from five independent colonies of wild rats in Warsaw, Poland (Stryjek & Pisula, 2008). To avoid inadvertent effects of domestication, wild rats caught at various locations were regularly added to the breeding stock, and testing was restricted to captive born subjects from the third generation of laboratory born subjects. The wild rats were bred and housed at the vivarium at the Institute of Psychology of the Polish Academy of Sciences (Warsaw, Poland). All animals were housed in Eurostandard Type IV cages (61 cm × 43.5 cm × 21.5 cm) with dust-free softwood granules (Tierwohl Super) as bedding; they were given constant access to water and standard laboratory fodder. The light-dark cycle was set at 12:12 with lights off at 20:00, and the temperature was maintained at a constant 21–23°C. All wild rats kept in the laboratory were housed, bred, and cared for in accordance with the Regulation of the Polish Minister of Agriculture and Rural Development of March 10, 2006, on laboratory animal care, and the experimental procedures were approved by the Second Local Ethics Commissions in Animal Experimentation (Warsaw, Poland). Although the study was conducted in two laboratories, it should be noted that previous studies have shown that strain differences in play behavior are robust across laboratories (Himmler, Lewis, & Pellis, 2014; Himmler, Modlinska, et al., 2014).

Procedure

For both strains, starting at around 24 days of age, each juvenile was housed with an adult (around 74 days of age). When the juveniles were between 30 to 35 days, play was tested. This is within the peak period for play behavior in rats (Meaney & Stewart, 1981; Pellis & Pellis, 1990, 1997; Thor & Holloway, 1984). For three days before testing play, all animals in their dyads were habituated to the testing enclosure for 30 min per day. A period of social isolation preceding testing is routinely used in studies of play with rats, as it has been shown to increase the frequency of play fighting during the test trial (Panksepp, 1981; Panksepp & Beatty, 1980; Niesink & van Ree, 1982). The present study used 24 hr of social isolation, as systematic comparisons have shown this time frame to increase the frequency of play to an optimal level for assessing the varied defensive actions possible during play fighting (Pellis, Field, Smith, & Pellis, 1997). Test trials lasted for 10 min each, providing enough time to capture most aspects of the playful interactions. Even though tested in the first 3 hr of onset of the light cycle, both habituation and testing occurred in complete darkness, as it has been shown that social behaviors such as play increase when in the dark as compared to light conditions (Himmler, Pellis, & Pellis, 2013). Play trials occurred in a 50 cm × 50 cm × 50 cm Plexiglas box encased in a soundproofed chamber (61 cm × 61 cm × 84 cm). The floor of the testing chamber had a 1-2-cm layer of bedding of processed corncobs for LE rats and Tierwohl Super bedding for WWCPS. After each trial, the boxes used were thoroughly cleaned with Virkon and the bedding was replaced to clear the experimental box from any smells of the previous occupants.

The play trials were recorded obliquely from the front (at 45°) using a DVD103 Sony Handycam for the LE rats and a BCS 0804LE-A DVR system for the WWCPS rats, with both cameras having night-shot capability. All six pairings of LE rats were successfully recorded, but only six of the eight trials with WWCPS were successful. In one pair, some inadvertent noise is likely to have occurred, as the pair remained immobile until the last 2 min of the trial. For the other pair, too little play occurred to be able to evaluate the various measures of play required by this study (see below). Therefore, cross-strain comparisons were based on six pairs of each strain.

Behavioral Analysis

Adult female WWCPS rats are significantly smaller than adult female LE rats (body weight, in grams: 165.0 vs. 276.0, from a sample comparable aged adult females in Williams ([2018]), a size difference consistent with the effects of domestication (King & Donaldson, 1929). Given that there was a similar size difference between the juveniles of the two strains, the adult pairmate in each

group was over twice as large (between 2.2-2.5 times larger). The size discrepancy has an impact on how easily some of the tactical maneuvers used for defense during play can be assessed (Pellis, Williams & Pellis, 2017; Pellis, Himmler, Himmler, & Pellis, 2018). In addition, strain differences in the frequency of playful attacks and in the defensive tactics that are used most often and how these are executed (e.g., Himmler, Himmler, Stryjek, et al., 2016; Himmler, Lewis, & Pellis, 2014; Himmler, Modlinska, et al., 2014; Himmler, Stryjek, et al., 2013) make it difficult to directly compare the frequency differences in particular playful maneuvers between the pairs of the two strains. As what was of interest in the present study was the relative asymmetry in the playful behavior between juveniles and adults across the two strains, novel indices derived from our standard scoring scheme for same-aged play in rats (Himmler, Himmler, Stryjek, et al., 2016; Himmler, Pellis, & Pellis, 2013) were developed (see below).

Playful attack. A playful attack was scored when the tip of the snout of one rat was either in contact with its partner's nape or when one made a targeted movement towards the nape of the other. As WWCPS rats launch fewer playful attacks than domesticated strains of rats, including LE rats (Himmler, Modlinska, et al., 2014; Himmler, Stryjek, et al., 2013), the total number of attacks per pair was scored to compare between strains (Prediction 1) and the proportion of those by the adult was calculated to ascertain whether the two strains were asymmetrical with regard to launching attacks (Prediction 2) and whether the relative asymmetry in playful attacks between strains differed (Prediction 5).

Playful defense. The recipient of an attack can respond to it by using one of many defenses or can simply ignore it (Himmler, Pellis, & Pellis, 2013; Pellis & Pellis, 1987). The first measure for comparison was the relative proportion of attacks being defended by an adult when attacked by a juvenile compared to that of a juvenile when attacked by an adult (A/A+J) (Prediction 3). When a playful attack is defended, two categories of tactics can be used: (a) evasion, which involves the defender moving its nape away from its attacker by running, jumping, or pivoting away, or (b) facing defense, in which the defender turns to face its attacker in order to block access to its nape by opposing its teeth between its partner and its own nape. Although facing defense can itself involve different tactics (Himmler, Pellis, & Pellis, 2013), body size differences in the participants can make such discriminations difficult (Pellis et al., 2017; Pellis et al., 2018). In addition, there are strain differences, with WWCPS rats defending more often by using evasion than LE rats and LE rats using the turning to supine facing defense tactic more often than the WWCPS rats (Himmler, Stryjek, et al., 2013). Therefore, for the present study, in which the adult partner was over twice as large as its juvenile partner, defense was simply scored as to whether it involved evasion. The initial 2-3 video frames from the onset of a defensive movement were used to determine if the recipient of the attack attempted an evasive maneuver whatever the eventual outcome of an attack (Himmler, Pellis, & Pellis, 2013).

In order to capture the age differences while minimizing the effects of strain differences when comparing the two strains, the relative proportion in which adults evaded playful attacks by juveniles compared to the proportion of evasion when juveniles were attacked by adults (A/A+J) was used (Prediction 4). All other defended attacks led to protracted close-quarter wrestling. The relative proportion of such wrestling was scored per pair irrespective of when it emerged in the encounter (Prediction 6).

Reciprocation. During play fighting, the defender may launch counterattacks, which, if successful, can lead to a role reversal, as the original attacker adopts a defensive role (Pellis & Pellis, 1987, 1990). Also, during the peak juvenile period, the animal in the dominant position is likely to adopt postures and perform movements that facilitate successful counterattacks (Pellis et al., 2005). Moreover, irrespective of strain-typical patterns of play fighting, in highly playful strains of rats, role reversals occur in about 30% of play fights (Himmler, Himmler, Pellis, & Pellis, 2016). The total frequency of role reversals was scored for each pair and this was converted to a percentage by dividing this number by the total number of defended attacks, as only defended attacks can lead to counterattack and so possible role reversal (Pellis & Pellis, 1987; Pellis, Pellis, & Dewsbury, 1989). The overall percentage of role reversals was calculated (Prediction 7), as was the percentage of those role reversals initiated by the juvenile partner (Prediction 8).

Statistical Analysis

All comparisons between the scores from pairs of the two strains were tested using independent *t*-tests. Even though multiple *t*-tests were conducted, the similarities and differences in the scores compared were predicted, so corrections to reduce the risk of Type 1 errors were not deemed necessary. Differences were considered significant for p values of ≤ 0.05 and, because the direction of the difference was predicted for measures of Predictions 1, 2, 5, 6, 7 and 8, this was a one-way test. Because the measures for Predictions 3 and 4 were predicted not to differ, this was a two-way test. For tabular representation of the data, values are given as group means and standard errors.

The data for the LE rats were consistent with the data previously analyzed for adult-juvenile pairs (Pellis et al., 2017). However, as the play of wild rats in such pairings has not been previously scored, the video records scored by one observer (SMP) were re-scored by another (VCP). The second scorer was not informed of the hypothesis being tested until after video scoring was completed. The scores between observers were significantly correlated, $r > 0.80$. Moreover, a qualitative assessment of the play of wild rat pairs by yet another observer (BTH) yielded a verbal description that was consistent with the numerical scores.

Results

All the predictions were supported (Table 1). The WWCPS pairs launched fewer nape attacks than did the LE rats (Prediction 1), and the adults launched a minority of the attacks in both strains (Prediction 2). The adults of both strains were less likely to defend themselves against nape attacks by the juvenile partners than were juveniles when attacked (Prediction 3), and adults of both strains were more likely to evade nape contact by the juveniles when they did defend themselves (Prediction 4). Despite the similarities in the responses of all adults to the juveniles' advances, there were differences in how WWCPS adults played with juveniles compared to LE adults. Even though the adults of both strains launched fewer nape attacks than their juvenile partners, WWCPS adults launched 3.4 times more attacks than LE adults (Prediction 5) and engaged juveniles in more wrestling contests (Prediction 6). A greater proportion of play fights by the pairs of WWCPS rats involved role reversals (Prediction 7), and WWCPS juveniles initiated a greater proportion of those role reversals (Prediction 8).

Table 1

Behavioral Comparisons Across Strains Associated with Different Predictions

Behavioral measurements	Long Evans	WWCPS	*t*-tests
Nape attacks per 10 min (P1)**	87.93 ± 21.92*	40.50 ± 18.95	$t = 4.00$ $p < 0.01$
Percent attacks by adults (A/A+J) (P2 & P5)	7.52 ± 6.64	25.86 ± 7.54	$t = -4.47$ $p < 0.01$
Percent of attacks defended by adult (A/A+J) (P3)	81.16 ± 10.59	76.72 ± 11.64	$t = 0.69$ $p > 0.05$
Percent of defenses involving evasion by adult (A/A+J) (P4)	66.53 ± 8.34	73.99 ± 16.51	$t = -0.98$ $p > 0.05$
Percent of play fights with wrestling (P6)	24.58 ± 11.65*	55.92 ± 16.62	$t = -3.78$ $p < 0.01$
Percent of play fights with role reversals (P7)	15.22 ± 5.75	23.46 ± 5.34	$t = -3.51$ $p < 0.01$
Percent of role reversals by juvenile (P8)	5.90 ± 9.25	31.02 ± 14.09	$t = -3.65$ $p < 0.01$

Note: *Mean ± standard deviation shown based on six pairs per strain; **The specific predictions related to each measurement are shown in parentheses. P = prediction.

An unexpected difference in behavior between WWCPS and LE adults became evident during the scoring of the play sequences. Most attacks are defended against, but some are not (Pellis & Pellis, 1987, 1990); this usually involves the recipient continuing with its ongoing behavior (e.g., exploring, self-grooming, etc.). Sometimes, however, the recipient stops its ongoing behavior and remains immobile. This immobility facilitated the juvenile's ability to gain access to the adult's nape. The cases in which the adult did not defend itself against a nape attack were re-examined in both strains and the percentage of cases in which the adult remained immobile was scored. Remaining immobile was more frequent in WWCPS adults than in LE adults (19.54 ± 14.69 versus 4.99 ± 6.25). Given that we had no a priori expectation for the direction of the difference between the strains, a two-tailed t-test was used to assess the difference, which revealed that the difference was significant ($t(10) = 2.23$, $p < 0.05$).

Discussion

Unlike the case in domesticated LE hooded rats (Bell et al., 2010; Himmler, Pellis, & Kolb, 2013), in wild rats, there is no difference in the pruning of the dendritic arbor of the neurons in the mPFC when juveniles are reared with either a juvenile or adult partner (Himmler, 2015). The hypothesis tested in the current paper is that this difference in the effects of rearing environment between the two strains of rats is that, unlike domesticated adult rats, the wild adults provide the juveniles with more opportunities for playful interactions that generate the reciprocal exchanges needed to promote the development of the mPFC (Pellis, Williams & Pellis, 2017; Pellis et al., 2018). All predictions derived from this hypothesis were confirmed (Table 1). Moreover, an unpredicted finding – that WWCPS adults were more likely to adopt postures that facilitate nape contact by the juveniles – further supports the hypothesis that wild adult rats, unlike domesticated ones, are more cooperative in their play with juveniles.

Converging data suggest that it is the opportunity to interject cooperative behavior within the context of competitive playful interactions that seems to be critical for modifying the mPFC and refining sociocognitive skills (Burleson et al., 2016; Pellis et al., 2017; Schneider, Bindila, et al., 2016; Schneider, Pätz, et al., 2016). Therefore, it is likely that the additional opportunities for wild juvenile rats to gain the experience of reciprocal cooperation, as seen by the greater frequency of juvenile-initiated role reversals, may account for the lack of difference in dendritic pruning of mPFC neurons in wild juveniles reared with either other juveniles or with adults (Himmler, 2015).

While the difference in degree of asymmetry in the playful interactions of the WWCPS and LE rats are consistent with the hypothesis, there are limitations in the data to consider. First, the sample sizes are relatively small, and, second, the two strains of rats were sampled at different times and locations by different experimenters. That the LE sample replicates a previous study (Pellis, Williams & Pellis, 2017) and that strain differences in play are robust across studies that encompass different locations, sources of animals, experimenters, and rearing and testing cages (e.g., Bell, McCaffrey, Forgie, Kolb, & Pellis, 2009; Himmler, Lewis, & Pellis, 2014; Himmler, Modlinska, et al., 2014; Pellis & Pellis, 1990; Smith, Forgie, & Pellis, 1998) provides evidence that the strain differences found in the present study are likely real. However, given that it is not just the strain-typical pattern of play, but the magnitude of the differences between the WWCPS and LE strains that are critical for the current hypothesis, it is important that future studies corroborate the present findings by testing the two strains concurrently in the same location and by the same experimenters.

Even if the strain differences in asymmetry are true, it remains to be determined if they are sufficient to account for the strain differences in the effects of rearing partner on the development of the mPFC. Given

that the absolute amount of play is lower in the WWCPS rats than in the LE rats (Table 1), it is important to try to estimate the actual number of reciprocal playful events that juveniles would experience over the critical developmental period. First, it is not the total number of nape attacks that need to be considered but the number of defended nape attacks, as this is what leads to competition and opportunities for role reversals (Pellis & Pellis, 1987). Taking this modified number, the number of play fights containing a role reversal can be calculated and then this can be further modified by only considering the role reversals initiated by the juveniles, as these would be the ones most likely to be important for training sociocognitive skills (Pellis, Williams & Pellis, 2017). Second, the resultant numbers need to be expanded to include what rats would experience over the whole day. Einon et al. (1978) based their manipulations of play in the juvenile period on findings that, over 24 hr, juveniles engage in play for about 1 hr. Since our trials were for 10 min, this needs to be corrected to what the number would be for 60 min, but, in turn, this number needs to be further corrected to make it a realistic estimate. In paired trials, the amount of play that occurs without preceding social isolation is about 40% of that which occurs after 24 hr of social isolation (Pellis et al., 1997).

Finally, in the actual rearing environment, individuals have daily exposure to potential play partners. Play is both most frequent during the peak juvenile period, 30-40 days post-birth (Thor & Holloway, 1984), the age in which reciprocity-facilitating maneuvers are most frequent (Foroud & Pellis, 2002) and the age period when social isolation seems most likely to have sociocognitive effects (Arakawa, 2002, 2003; Einon & Morgan, 1977). Therefore, starting with the difference found in the present study (Table 1) and applying the above described factors to evaluate the total number of juvenile-induced role reversals likely experienced over this critical period of 10 days, WWCPS juveniles would experience more than LE juveniles would (54.3 vs. 15.4). Moreover, given the longer juvenile period in wild rats (Clark & Price, 1981), this 3-4 times difference may be an underestimate.

It should be noted that for Wistar rats reared with Fischer 344 rats, in which, like our adult females, the Fischer rats provide fewer opportunities for reciprocal play, the reduced role reversals available to the Wistar rats were similar in staged paired encounters and in spontaneously occurring play in the home cage (Schneider, Bindila, et al., 2016; Schneider, Pätz, et al., 2016). These similarities suggest that the above calculations are not unreasonable, showing that over the most important phase of the juvenile period, WWCPS juveniles experience about 39 more juvenile-induced role reversals than LE juveniles do. The important question is whether so seemingly few extra experiences with role reversals are sufficient to account for the differences in the development of the mPFC between the two strains.

The magnitude of the pruning present in wild rats from either rearing condition is much greater than the level of pruning present in LE rats reared with other juveniles (see Figure 12.3, p. 325 in Pellis et al., 2018). It is possible that there are strain differences in neural plasticity, requiring different degrees of experience to produce comparable changes in neural organization. For example, behaviorally, domestic rats jump less than wild rats, irrespective of whether they are reared in a restricted, standard cage or in an enriched environment (Huck & Price, 1975). Whereas the climbing ability of domestic rats is dependent on being reared in cages that offer opportunities for climbing, that of wild rats does not (Huck & Price, 1976). Moreover, there are both behavioral and neural differences across domestic strains of rats (e.g., Himmler, Modlinska, et al., 2014; Keeley, Bye, Trow, & McDonald, 2015; Modlinska, Stryjek, & Pisula, 2015; Stryjek, Modlinska, Pisula, 2012). In a comparison across three strains (including WWCPS rats) of both the cerebellum and other subdivisions of the brain (including the cortex) there were overall strain differences in some measures of cell numbers, cell sizes, and volumes of specific regions (Williams, 2018). Critically, for the current issue, one strain, LE hooded, showed consistently greater variability across many of the measures than the other two strains (WWCPS and Sprague Dawley) (Williams, 2018). The greater variability across individuals in one

strain over others may reflect strain differences in how plastic those neural systems may be, with small experiential differences across individuals producing differences in neural organization.

The effect of play with peers on neural development and sociocognitive development in the juvenile period has been demonstrated across several of rat strains (Baarendse et al., 2013; Bell et al., 2010; Einon et al., 1978; Himmler, Pellis, & Kolb, 2013; Himmler et al., 2018; Schneider, Bindila, et al., 2016; Schneider, Pätz, et al., 2016; van Kerkhof, Damsteegt, Trezza, Voorn, & Vanderschuren, 2013) and across species (Burleson et al., 2016; Marks et al., 2017). However, the threshold level of experience needed may differ. It is possible that, in WWCPS rats, the mPFC is more responsive to juvenile play experiences, so that a modest increase in juvenile-induced role reversals may be sufficient. In contrast, the LE rats may require more such experiences to produce an equivalent change in the mPFC. Systematic comparative studies are needed.

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