Investigating the link between the rodent posterior parietal cortex and sociality

By

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Thesis

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I would like to thank Brown University as well as Providence College for use of resources required to conduct this study.

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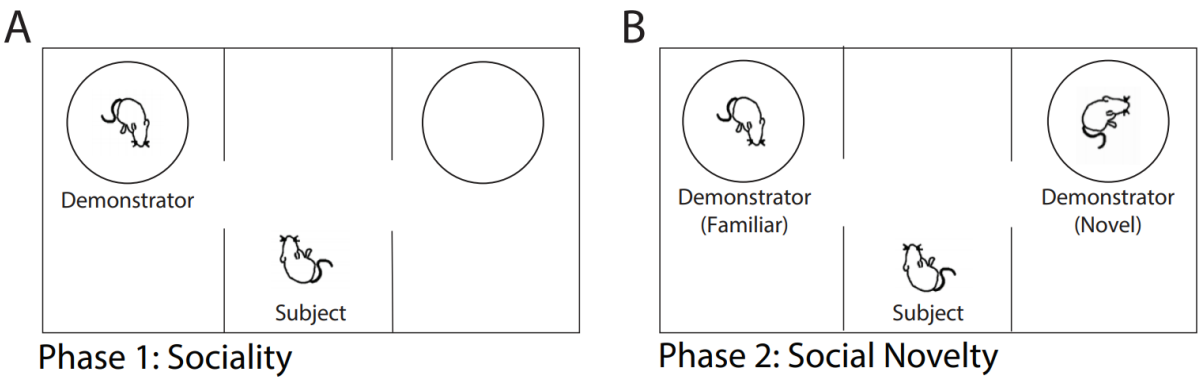


Figure 1. 3-Chamber Sociability and Social Novelty task. A) Phase 1- Sociability test in which the subject rat is free to explore a demonstrator rat and an empty cage for 10 minutes. B. Phase 2- Social Novelty test in which a familiar demonstrator rat (continued from Phase 1) is presented along with a novel demonstrator and subject is free to explore for an additional 10 minutes. ITI was approximately 2 minutes between phases.

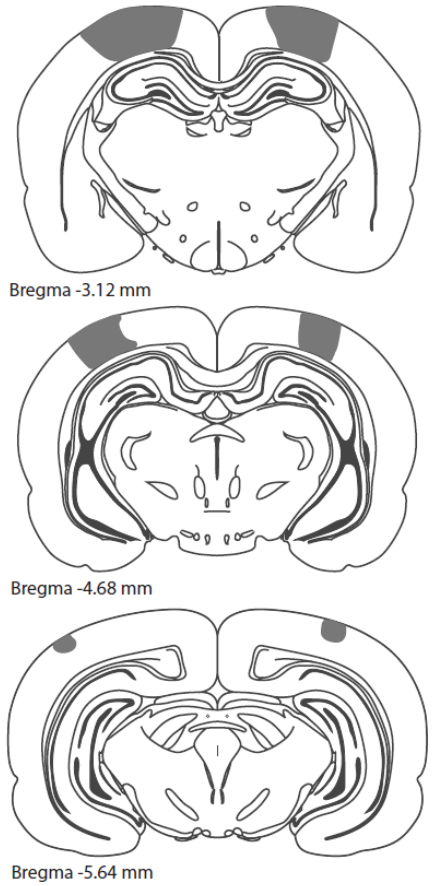
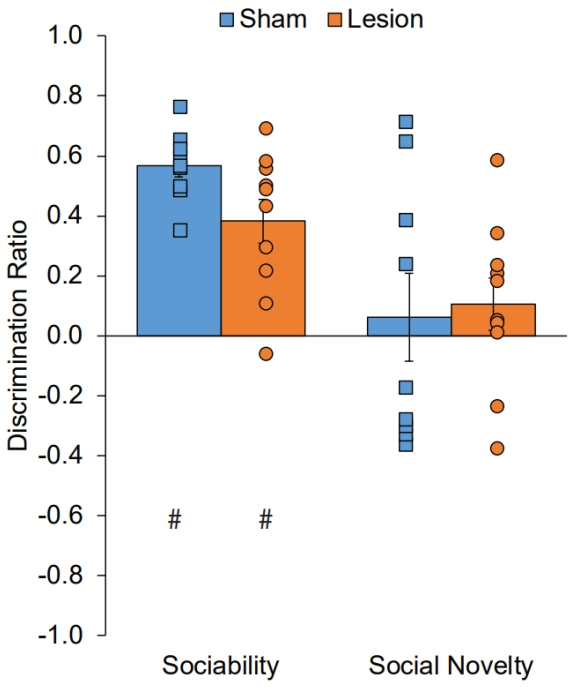


Figure 2. Coronal sections showing representative areas (shaded in gray) affected from NMDA lesion to dPPC.



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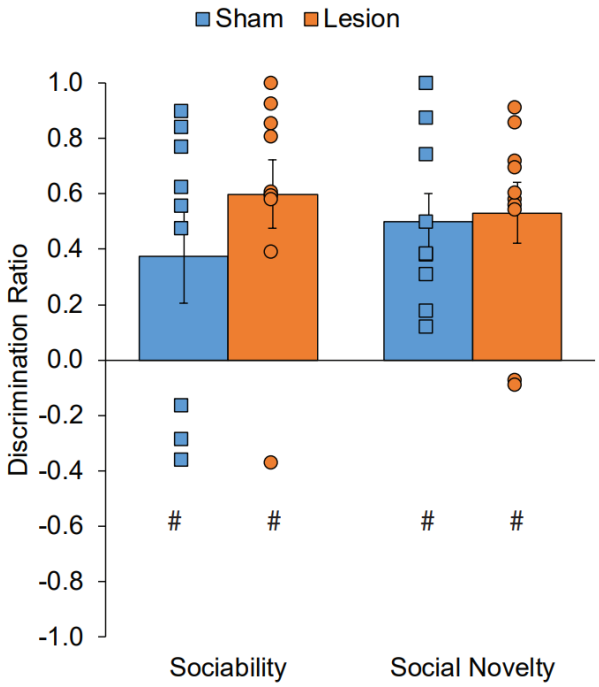

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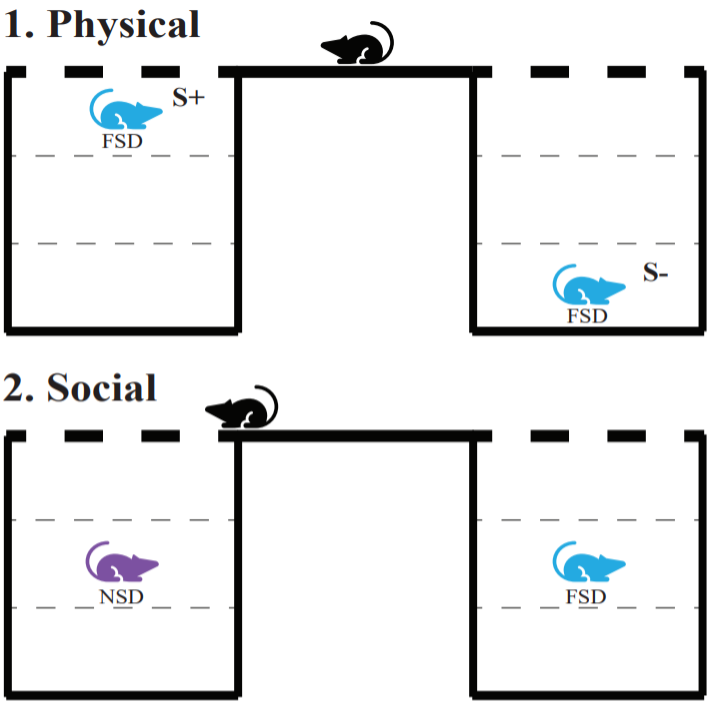

Figure 5. Physical-Social transfer task. In this paradigm rats are trained to discriminate physical distances and then transfer learned information onto a social probe. 1. Physical: Subject is rewarded when selecting near physical distance (FSD). 2. Social: Subject must select the near social distance demonstrator (NSD), their cagemate.

ABSTRACT OF INVESTIGATING THE LINK BETWEEN THE RODENT POSTERIOR PARIETAL CORTEX AND SOCIALITY

BY TAYLOR WISE, ScM,

BROWN UNIVERISTY, MAY 2020

Recent literature points to a potential link between the evolution of complex social behavior and the posterior parietal cortex (PPC) in primates including humans (Parkinson & Wheatley, 2013). Thus far, this theory has been overlooked in other highly social animals that may have also evolved due to social selective pressures. We investigated the role of the PPC through two experiments that utilized that 3-Chamber Sociability and Social Novelty test in rats. In Experiment 1, subjects explored two novel demonstrators, a methodology common in prior literature. In Experiment 2, subjects explored a highly familiar cagemate and novel demonstrator, increasing novelty difference between social stimuli. Both experiments showed that all rats preferred general social interaction in Phase 1, suggesting no deficit in sociability following PPC damage regardless of demonstrator identity. Results from Phase 2 of Experiment 1 and 2 showed significant increase in social novelty preference for all rats when increasing demonstrator's difference in familiarity. Within the confines of the 3-Chamber task, our results suggest that PPC function was not required for general sociability or social novelty recognition; however, by manipulating the identity of demonstrator rats, novelty preference was impacted. Future studies should investigate the role of the PPC in social cognition by employing behavioral tasks that require a higher cognitive demand and specifically address spatial and social mechanisms.

Introduction

Throughout evolutionary history humans have relied on social structures for survival and have built complex cognitive systems to maintain such relationships. Selective pressures have molded the human and non-human primate brain to manage the intricacies of social living, and it is likely that, along with these structural changes, the supporting neural mechanisms have also evolved. However, how this mechanistic change occurred has yet to be explained. Further, it is still unknown how social cognition evolved despite an extensive record of primate cortical development. Recent theories investigating the topic of sociocognitive evolution posit that the primate brain has been equipped to understand social relationships through a process known as *exaptation*. Through exaptation, a specific region of the brain originally used to manage one aspect of cognition undergoes a cortical repurposing in order to meet new cognitive demands (Anderson, 2010; S. J. Gould, 1991). Specific to social cognition, scientists predict that a key region to be cortically repurposed in response to social needs was the posterior parietal cortex (PPC) (Parkinson & Wheatley, 2013; Yamazaki, Hashimoto, & Iriki, 2009).

The PPC has been investigated across multiple species, with an emphasis on its role in spatial cognition (Kesner & Creem-Regehr, 2013; Mohan, de Haan, Mansvelder, & de Kock, 2018; Nitz, 2006). It has been shown that the PPC is responsible for spatial processing including knowledge on spatial position (Snyder, Batista, & Andersen, 2000), direction of movement and locomotor behavior (Chen, Lin, Green, Barnes, & McNaughton, 1994; Nitz, 2012; Steinmetz, Motter, Duffy, & Mountcastle, 1987), as well as required for tracking route progression (Nitz, 2006; Rodriguez, 2010; Wilber, Clark, Forster, Tatsuno, & McNaughton, 2014). Further, work from the Nitz Lab has shown that a variety of neural inputs recorded in the rat converge on the

parietal cortex to integrate information relevant to spatial navigation, a commonality among many regions implicated in spatial cognition (Nitz, 2006, 2012).

A secondary emphasis on the PPC has been its link to attentional processes as it relates to space (Colby & Goldberg, 1999; Posner, Walker, Friedrich, & Rafal, 1984; R. L. Reep & Corwin, 2009). Examining the effects of PPC damage in human and non-human primates has shown that it is difficult for subjects to disengage attention from one visual stimulus to engage with another (Farah, Wong, Monheit, & Morrow, 1989; Petersen, Robinson, & Currie, 1989; Posner et al., 1984). This impairment in attentional set shifting has also been shown in rodents where lesioned animals had difficulty abandoning their attention from the initial stimulus dimension in a multi-dimensional learning task (Fox, Barense, & Baxter, 2003). Two major regions, the dorsal (dPPC) and caudal PPC (cPPC), show a functional difference in top-down and bottom-up attentional processes, respectively (Bressler, Tang, Sylvester, Shulman, & Corbetta, 2008). In the primate PPC, it has been shown that the dPPC is specifically implicated in top-down attention used to guide goal-orientated behavior, whereas the cPPC is implicated in bottom-up, stimulus driven attention (Shomstein, 2012).

With support from these studies it has been argued that a functional homolog of the PPC exists across human and non-human primates (Campbell & Hodos, 1970). In humans, the PPC consists of the superior parietal lobe (SPL; Brodmann Area 5) and the inferior parietal lobe (IPL; Brodmann Area 7), separated by the intraparietal sulcus. A similar anatomy is found in the monkey PPC with a defined SPL and IPL (Cavada & Goldman-Rakic, 1989a, 1989b). Research on this potential homolog has been extended to rodents and considerable work has been dedicated to understanding the rat PPC. In both primates and rats the PPC has been anatomically defined (Kolb & Walkey, 1987; Krieg, 1946; R. L. Reep, Corwin, Hashimoto, & Watson, 1984)

as well as the thalamic regions that supplement the PPC for both species (Baleydier & Mauguiere, 1987; Chandler, King, Corwin, & Reep, 1992; Gutierrez, Cola, Seltzer, & Cusick, 2000; R. Reep, Chandler, King, & Corwin, 1994; Yang, Jacobson, & Burwell, 2017). Further, scientists have begun to define subregions of the rat PPC that may be functionally analogous to its primate counterpart (Palomero-Gallagher & Zilles, 2015; Pérez-Clausell, 1996; Swanson, 2004). There is still much to be learned however on the coordinates and functions dividing the rat dPPC and cPPC. With supportive electrophysiological and experimental lesion evidence it can be argued that the rat is an ideal translational model for understanding the primate PPC.

While many studies investigating the PPC have focused on its spatial and attentional responsibilities, there is a subset of the literature that has explored its ties to social cognition. Parkinson & Wheatley (2013) argue that the exaptation theory may be important in understanding how the PPC relates to social cognition given our ancestors' selective pressures towards group living. This is supported by research that shows mechanisms devoted to spatial knowledge are co-opted to process abstract cognition including social cognition (Chiao et al., 2009; Yamakawa, Kanai, Matsumura, & Naito, 2009; Yamazaki et al., 2009). In Yamakawa et al. (2009) subjects undergoing an fMRI task showed similar activation of the PPC when making physical distance judgements and social compatibility, otherwise known as "social distance", judgments. Interestingly, in a follow-up experiment where subjects placed dolls representing themselves and other people on a board, those deemed compatible were placed by participants in closer physical proximity to their personal doll. Combined, this suggests that the neural mechanisms supporting our understanding of physical distance is similar to our perception of social distance and that the PPC is recruited in both cases.

The social cognition literature mentioned has exclusively studied PPC function in human and non-human primates with no recognition yet given to rodent models. This is despite their anatomical similarities as described above. Given their excellent spatial navigation and ease in attentional tasks, rats have long been used to study cognitive processes that may employ the PPC (Bucci, 2009; Nitz, 2006). Yet unfortunately it is overlooked that rats are also highly social animals. In the lab, rats have been shown to prefer social over non-social interactions (Douglas, Varlinskaya, & Spear, 2004; Peartree et al., 2012; Templer, Wise, Dayaw, & Dayaw, 2018; Van Loo, Van de Weerd, Van Zutphen, & Baumans, 2004) and are highly motivated by social reward (Kummer et al., 2011; Thiel, Okun, & Neisewander, 2008; Vanderschuren & Trezza, 2013; Varlinskaya, Spear, & Spear, 1999). Further, rats in the wild live in large social groups (Barnett, 2017) highlighting the ecological relevance of social cognition. It is possible that survival in these groups requires knowledge of complex social dynamics that may implement regions such as the PPC.

A validated task for studying rat social behavior, the 3-Chamber Sociability and Social Novelty task, measures subjects' preference for social versus non-social experiences as well as social novelty (Crawley, 2004). Otherwise known as Crawley's Test, this behavioral paradigm is widely accepted within the literature and has been used to research topics ranging from autism, to drug use, to aging (Bambini-Junior et al., 2014; G. G. Gould et al., 2012; Jaramillo, Liu, Pettersen, Birnbaum, & Powell, 2014; S. Moy et al., 2004; S. S. Moy et al., 2013; Templer et al., 2018). Given its well replicated results, we utilized this task to explore PPC function. To better understand how the rodent PPC relates to social cognition it is vital to begin this investigation with a trusted behavioral task. To our knowledge, this study is the first to manipulate PPC

function not only in the 3-Chamber test, but also in the in general across the rat literature as it relates to sociality.

In this study, we explore the role of the PPC as it relates to social behavior and cognition in the rat model. To test for the PPC's influence on social cognition, we manipulated its function through neurotoxic lesions, and tested subjects on the 3-Chamber Sociability and Social Novelty Test in two experiments. In Experiment 1 we conducted the standardized 3-Chamber task typically used to understand rodents' social preferences. This includes the use of two non-subject, demonstrator rats as stimuli. In Experiment 2 we manipulated the level of familiarity between demonstrator rats to magnify potential differences in novelty preference. Results did not reveal lesion effects in either experiment; however increased difference in familiarity in Experiment 2 did alter both sham and lesioned subjects' social behavior. Overall, we argue that while the 3-Chamber task appropriately examines social preference, it is incapable of decoding more cognitively demanding behaviors required to understand animals' perceived social distance. Therefore, a novel task is required to better investigate rodent PPC exaptation and these future directions are laid out in detail at the end of this paper.

Experiment 1: Standard Paradigm

LESIONS

Experimental rats received permanent neurotoxic lesions of the dPPC whereas the control rats received sham surgeries. All rats were anesthetized with isoflurane and secured in a stereotaxic frame. Once secured, the incisor bar was adjusted such that bregma and lambda were in the same horizontal plane (±0.2 mm) and rats' skulls were in flat position. Using a dental drill,

dura was removed, and a glass pipette (45-50 µm tip) was inserted into the target brain region (AP: -3.6 to -5.64; DV: -.05 to -1.1) (Olsen & Witter, 2016). Neurotoxic lesions were made using 0.09M NMDA (Tocris Bioscience, Minneapolis, MN) in 0.1M phosphate buffer. NMDA was drawn through a glass pipette and then delivered by pressure injection at 0.1 µL/min for one minute at each of the five bilateral sites. Following injections, the pipette was left in place for three minutes then slowly retracted. For sham surgeries, rats received craniotomies, but had no penetration of cortex. For all surgeries, skin was sutured, and rats were able to recover for at least one week prior to handling and behavioral testing.

BEHAVIORAL METHODS

All test sessions took place inside a three-room, social interaction chamber (30x45in, Noldus Technologies), known as the 3-Chamber Sociability and Social Novelty Test (Crawley, 2004; Kaidanovich-Beilin, Lipina, Vukobradovic, Roder, & Woodgett, 2011). Rooms were separated by two opaque doors that were removed to initiate the beginning of a test phase. The left and right rooms contained holding cages for demonstrator rats (Figure 1). Live tracking via Ethovision was present during all trials where cumulative sniff duration and frequency of visits to each demonstrator rat were measured. To habituate, subjects could freely explore the entire apparatus for five minutes. No demonstrators or holding cages were present during habituation. If subjects did not display anxious behavior, such as increased grooming, freezing, or defecation, they began Phase 1 approximately 24 hours following habituation. If anxiety was observed, habituation was repeated once a day until behavior was extinguished. Demonstrator rats also received 5-minute habituations to their holding cages prior to testing to ensure that they were comfortable with being confined and would not alter subject behavior.

[INSERT FIGURE 1]

Phase 1: Sociability Test. Round holding cages were placed at one end of the left and right rooms (Figure 1A). One cage contained a demonstrator rat unfamiliar to the test subject while the other cage was empty. Demonstrator/empty cage side was counterbalanced across subjects. To initiate the trial, subjects were placed in the center and doors to the left and right rooms were removed, allowing for exploration of the entire apparatus. The subject could interact with both the novel demonstrator rat and the empty cage as often as desired. Holding cages consisted of evenly spaced bars that allowed demonstrator and subjects rats to sniff and see each other while limiting physical contact. Sniff duration to the demonstrator/empty cage was coded by a blind experimenter in real time through the Ethovision software. Opaque walls prevented the subject from seeing either cage until entering the respective room. Subjects received a single 10-minute trial.

Phase 2: Social Novelty Test. Immediately following Phase 1, subjects were returned to the center room and the doors to either side were closed for an ITI of two minutes. A second unfamiliar rat was placed in the previously empty holding cage while the demonstrator from Phase 1 (now familiar) remained in position (Figure 1B). Designated familiar and novel demonstrators were counterbalanced across subjects. Doors were then removed, and subjects were free to explore for an additional 10 minutes. Identical in form to Phase 1, data was coded by a blind experimenter via Ethovision. Once testing was complete, all rats were returned to their home cages and the apparatus was cleaned to eliminate odor transfer between subjects.

DATA ANALYSIS

As described above, data was coded blindly and then extracted from Ethovision. Sniff behavior toward the empty cage and all demonstrators was used to calculate a discrimination ratio (DR) where [DR=(Novel-Familiar)/(Novel+Familiar)] (Ennaceur & Delacour, 1988). Discrimination ratios are used to depict complex behavioral data through a single measure, accounting for, in this case, exploration to an empty cage and all demonstrator rats. In the experiments of this study a DR of (+)1 is equal to complete preference for the demonstrator in Phase 1 and for the novel demonstrator in Phase 2; a DR of (-)1 is equal to complete preference for the empty cage in Phase 1 and for the familiar demonstrator in Phase 2. Outlier analysis was conducted for all data where outliers were replaced with the mean value of the group and results were analyzed via SPSS.

Results- Experiment 1

LESIONS

Prior to behavioral testing, subjects received either permanent neurotoxic lesions of the PPC (n=9) or sham surgeries (n=10). In the experimental group, rats were administered a 0.1 µL NMDA injection at 5 bilateral sites (Olsen & Witter, 2016). A dPPC deficit was achieved with mean percent damage in the left hemisphere of 78% (SD=18.25) and 88% spread (SD=13.63), and in the right hemisphere 77% (SD=16.24) damage and 88% (SD=12.12) spread. Coronal sections illustrating the area affected is shown in Figure 2.

[INSERT FIGURE 2]

BEHAVIORAL RESULTS

In Experiment 1 rats were tested on the standard 3-Chamber Sociability and Social Novelty task. In this paradigm rats were free to explore a novel demonstrator and an empty cage in Phase 1, and two demonstrators, one that is familiar, in Phase 2. Subjects' sniff behavior to stimuli was the primary measure of exploration and converted into discrimination ratios.

For Phase 1, both sham and lesioned rats preferred to spend more time with the demonstrator rat as compared to the empty cage (Figure 3). Discrimination ratios for both groups were significantly different from zero (One-sample ttest: $t=4.374$, $p=0.002$ for shams; $t=7.654$, $p=0.000$ for lesions) and no group difference in DR scores were shown (Paired-samples ttest: $t=-0.545$, $p=0.600$). Together this shows that PPC lesions did not affect rats' general sociability preferences. In Phase 2, neither group showed a significant preference for either the novel or familiar demonstrator rat, as shown through the discrimination ratios (One-sample ttest: $t=0.891$, $p=0.443$ for shams; $t=0.516$, $p=0.265$ for lesions; Figure 3). Again, no group difference in DR scores was shown (Paired-samples ttest: $t=0.562$, $p=0.589$). It would be expected that sham animals in this experiment should replicate behavior shown in previous literature, where normal functioning rats prefer social novelty. For this reason, potential theories on these results are discussed in more depth in our Discussion below.

[INSERT FIGURE 3]

Our results from Phase 1 show that when rats were free to explore a novel demonstrator and an empty cage, all subjects preferred the social experience. This was true regardless of damage to the PPC. In Phase 2, when allowed to interact with a novel and familiar demonstrator, no group showed significant novelty preference. Due to sham animals' nonsignificant DR score we cannot sufficiently claim that lesioned rats' social novelty preference was affected by the

PPC. Importantly, no difference in total exploration was found in either phase when comparing sham and lesioned animals and is thus not thought to be responsible for shams' unexpected behavior.

Experiment 2: Increased Familiarity Paradigm

METHODS

All methods and analyses were identical to those described in the Standard paradigm apart from introducing subjects to new demonstrator rats. In the previous experiment, each demonstrator was unfamiliar to the subject prior to testing. In Experiment 2 however, the demonstrator in Phase 1 (thus the familiar demonstrator in Phase 2) was replaced with a cagemate. Subjects were housed with their cagemate for approximately 10 months prior to testing, providing ample opportunity to interact socially. This paradigm was conducted to exaggerate the difference in familiarity between demonstrators, providing an opportunity to examine PPC function in social interaction during varied degrees of presumed familiarity. Like in Experiment 1, a habituation process was conducted prior to testing. First, subjects were given a 5-minute habituation in which they could explore the entire apparatus void of any non-subject rats or holding cages. A second habituation was conducted where subjects could explore their cagemate located inside the holding cage. This served to prevent subjects' possible anxiety by observing their cagemate in confinement. Approximately 24 hours after habituation, Phase 1 and Phase 2 were conducted under the same time limits shown in the Standard paradigm. While habituation was intended only to diminish potential stress from seeing a cagemate in confinement, primary results showed that all subjects behaved in this event as would be expected

in Phase 1. In the planned Phase 1, following habituation, it was shown that social interaction had been nearly extinguished. For this reason, the results we present are from rats' first experience with their cagemate and will from here forward be referred to as Phase 1, Sociability. To ensure that the 5-minute Phase 1 trial was a true comparison to the 10-minute Phase 2 trial, we analyzed discrimination ratio data from Phase 2 at the 5- and 10-minute mark. In a paired-sample ttest of 5- versus 10-minute data in Phase 2, we found that there was no significant difference in behavior ($t=-0.880$, $p=0.405$ for shams; $t=-0.431$, $p=0.678$ for lesions). Due to this non-significant difference, we will be comparing the complete time rats spent exploring the apparatus in Phase 1 (5 minutes) to the maximum time of Phase 2 (10 minutes).

RESULTS

In Experiment 2, rats were again tested on the 3-Chamber task, yet now with a manipulation to increase the difference in familiarity between demonstrator rats. Experimental design was replicated from Experiment 1 with the exception that the demonstrator in Phase 1 (and thus the familiar demonstrator in Phase 2) was replaced with the subject's cagemate. Because lesioned rats did not prefer social novelty in Experiment 1, substituting the demonstrator with a cagemate better examined the extent of the PPC's role in social novelty preference. It was hypothesized that by increasing the difference in familiarity between demonstrators in Phase 2, novelty preference would increase, and results may shed light on the level of influence the PPC has over perceived social novelty.

For Phase 1, rats explored their cagemate, still confined in a holding chamber, and an empty cage. Both sham and lesioned rats preferred their cagemate with DR scores significantly

different from zero (One-sample ttest: t=2.282, p=0.052 for shams; t=4.758, p=0.001 for lesions) and no group difference (Paired samples ttest: t=-0.778, p=0.459; Figure 4). As shown in Experiment 1, all rats preferred to socially interact with a conspecific over an empty cage, even if they experience the demonstrator regularly. In Phase 2, both sham and lesioned subjects preferred to socialize with the novel demonstrator over their cagemate, as shown through DR scores significantly different from zero (One-sample ttest: t=4.205, p=0.003 for shams; t=5.342, p=0.001 for lesions; Figure 4). No group difference was found between DR scores (Paired-samples ttest: t=-1.626, p=0.143). It should also be noted that no group difference in total exploration was found ensuring that results have not been skewed by disparities in overall subject participation.

[INSERT FIGURE 4]

Overall, Experiment 2 investigated the potential difference in sociability and social novelty preference when a demonstrator rat was replaced with an extremely familiar cagemate. In Phase 1, all rats still preferred socialization over nothing, despite the fact that they had ample opportunity to interact with their cagemate outside of the task. When increasing the difference in familiarity between demonstrator rats in Phase 2, it was found that both sham and lesioned subjects preferred the novel demonstrator over their cagemate. Compared to Experiment 1, lesioned rats now showed a significant novelty preference when a large difference in familiarity was present. This suggests that the PPC does not indiscriminately decrease social novelty preference, and rather that it is reliant on the level of comparative novelty between the available social options.

Discussion

In this study we explored rats' PPC function as it relates to social cognition. We hypothesized that, if the PPC plays a role in social cognition, lesioned animals would show decreased sociability and social novelty preference in the 3-Chamber task. Through two experiments we recorded sham and lesioned rats' social behavior, first in a paradigm standard to the literature and second in a paradigm that manipulated the difference in familiarity between non-subject demonstrator rats. Using sniff behavior as a measure of exploration, discrimination ratios were calculated for each experiment to illustrate subjects' social preferences.

In Experiment 1 we conducted the 3-Chamber task with one unfamiliar demonstrator in Phase 1 and a second unfamiliar demonstrator in Phase 2 (Figure 1). In Phase 1, where subjects could explore an unfamiliar demonstrator and an empty cage, both sham and lesioned animals preferred the demonstrator, suggesting that PPC deficits did not affect rats' affinity for social interaction. This result is not too surprising given that no literature has yet shown that the PPC is required for general sociability, and instead that it is active when making judgements between potential social partners (Chiao et al., 2009; Yamakawa et al., 2009). In Phase 2, where subjects could explore a familiar demonstrator (known from Phase 1) and an unfamiliar demonstrator, both groups showed no preference for either rat. In prior literature it has been shown that normal-functioning rodents exhibit a high social novelty preference (Crawley, 2004; Templer et al., 2018); however, this result was not replicated in our sham animals. There are a few possibilities for these deviated results including an adverse response to the novel demonstrator or heightened interest in the familiar demonstrator. While subjects could never make full-body contact with demonstrators, the holding chamber bars were far enough apart to allow for nose-to-body contact. It has been shown that even when body contact is blocked by barred holding chambers

or a mesh wall, rats will respond to the presence of a conspecific (Peartree et al., 2012). Therefore, if specific demonstrators gave off either positive or negative signals it could elicit a behavioral response from the subject. To ensure that these possible confounds did not affect future experiments, new demonstrators were used in Experiment 2. Given this discrepancy with our sham animals we cannot claim that lack of social novelty preference in lesioned rats was due to a PPC deficit.

The 3-Chamber task was again conducted in Experiment 2 with a critical manipulation to the level of familiarity between demonstrator rats. In the Increased Familiarity paradigm, subjects were exposed to a cagemate in Phase 1, and then again Phase 2 alongside a novel conspecific. Where in Experiment 1 demonstrators only differed in familiarity by the 10 minutes, this experiment examined social novelty preference when a stark difference between the subjects' options existed. To our knowledge this paradigm has yet to be studied and thus provides new insight on how rats respond to highly familiar versus novel social conditions. We hypothesized that when manipulating the difference in familiarity between demonstrators, subjects would alter their social behavior observed from Experiment 1.

In Experiment 2 Phase 1, where subjects were presented with their cagemate and an empty cage, both sham and lesioned animals preferred their cagemate. Like Experiment 1, this suggests that irrespective of normal PPC function, rats preferred social over nonsocial experiences. While we did not see PPC effects in Phase 1 for either experiment, it does support the fact that rats are highly social. Especially regarding Experiment 2, all animals preferred to be social even when their demonstrator was a cagemate, someone they were highly familiar with and had full-time access to outside of the task. This highlights rats' strong desire for social

stimulation and provides support for the argument that rodent social behavior is not only ecologically relevant, but also worth investigating.

In Phase 2, where subjects were presented with their cagemate and a novel demonstrator, both sham and lesioned rats preferred to spend more time in the novel context. This suggests that the PPC does not play a role in social novelty preference when demonstrator rats exhibit a large difference in familiarity. In theory, this increased difference in demonstrator familiarity should make for a heightened social novelty preference in normal-functioning rats, which we observed. Interestingly we observed this novelty preference in lesioned animals as well. It could be the case that, despite PPC disfunction, the level of novelty was high enough to compensate for any neural deficits. If we were to make claims about lesioned animals' behavior from Experiment 1, the interpretation would be that the Standard paradigm required a higher recognition capacity as compared to the Increased Familiarity paradigm (Experiment 2). It would have been more difficult for lesioned rats to discriminate between demonstrators in Experiment 1, thus explaining their lack of social novelty preference (Figure 3). It should also be noted that sham subjects' social novelty preference in Experiment 2 replicates prior literature, thus supporting our claim that subjects' unexpected behavior in Experiment 1 may have been due to a positive or adverse response to specific demonstrators and not inherent social deficits.

Overall, both experiments show no group differences between sham and lesioned subjects' behavior. This is true for both general sociability (Phase 1) and social novelty preference (Phase 2). Experiment 2 provides particularly interesting results given its novel methodology. Even with a high familiarity to their cagemate in Phase 1, subjects still chose a social experience rather than a nonsocial one, pointing to rats' general inclination towards sociality. This strong social nature may even outweigh neural deficits, given that we observed no

differences in behavior for lesioned animals. Further, when manipulating the difference in demonstrators' familiarity, social novelty preference in Phase 2 was altered in both groups. Not only does this suggest that PPC damage did not impact novelty preference or recognition, but also that the identity of a conspecific matters. While both experiments possessed a familiar demonstrator, our dissimilar results between the paradigms point to the importance of prior social knowledge of a conspecific when assessing rats' social preferences. It is possible that if the level of familiarity was to be titrated even further, we would observe a gradient of social preference or recognition. A focus on demonstrators' familiarity to the subject should be included in future studies to better understand the intricacies of rats' social cognition and behavior.

Future Directions

From this study we did not observe any behavioral difference between sham and lesioned animals in terms of sociability or social novelty preference. On the surface this may appear to suggest that the rodent PPC is not implicated in social cognition. However, given that the demands of social cognition are complex and not well understood it can be argued that the 3-Chamber task is simply not equipped to measure these processes. The potential role for the PPC in rodent social cognition has yet to be explored in any study outside of the one described here. For this reason, we felt that the investigation must begin with a task widely used and trusted in the field. The benefits of conducting the 3-Chamber task include ease of comparability between our lesioned animals and prior research. Yet importantly, we are the first to explore 1) PPC function in the 3-Chamber test and 2) the PPC-social cognition link in rodents; thus, the value of these comparisons is limited. While we cannot conclude that the PPC is required for rats' social

cognition from our experiments, we can state that this brain region is not implemented in social *preferences*. At the core of the 3-Chamber task, it is a passive test of behavior that never requires rats to learn or maintain extended knowledge of the quality of their social relationships. Of the research that has examined social functions of the PPC thus far in humans and primates, it always has involved higher order understandings of social networks and ego-centric bonds. Due to this methodological disparity, we argue that to better understand possible PPC expiation in rats we must employ a behavioral task that demands high-level cognitive functions of social knowledge. In future experiments we plan to examine the potential mechanistic overlap of spatial and social cognition through a novel task. In this task rats will be required to first learn to discriminate between near and far physical distances (Figure 5A). The stimuli at the end of each distance will include two demonstrator rats. Importantly, to discourage social novelty preference, subjects will be given familiarization sessions with their demonstrators prior to testing. Once discrimination of physical distance is learned, rats will receive a transfer probe where spatially the demonstrators are equal, but critically, the identify of demonstrators has changed. In the transfer probe, one demonstrator will remain at the level of familiarity as previously held during the physical distance discrimination, whereas the second demonstrator will be replaced with the subject's cagemate. Due to the higher familiarity of a cagemate as compared to the other demonstrator, there will be a distinct difference in social distance. It is hypothesized that if rats use the same mechanisms to understand spatial cognition as they do social cognition, subjects will be able to transfer knowledge of physical distance onto a social context.

[INSERT FIGURE 5]

In this study, we took the initial steps required to examine the rodent PPC as it relates to social cognition. Through the 3-Chamber Sociability and Social Novelty task we did not observe

any PPC deficits; however, we did find that when manipulating the level of familiarity, or social distance, rats' social novelty preference increased. In future experiment we plan to continue this investigation of the overlap of rats' spatial and social knowledge through a novel paradigm and apparatus. If the paradigm's transfer probe is successful in normal-functioning rats we plan to next manipulate PPC function in this task.

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