RESEARCH REPORT

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Lesions of nucleus accumbens shell abolish socially transmitted food preferences

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Abstract

Rats adapt their food choices to conform to their conspecifics' dietary preferences. The nucleus accumbens shell is a relevant brain region to process reward-related and motivated behaviours and social information. Here, we hypothesize that the integrity of the nucleus accumbens shell is necessary to show socially transmitted food preferences. We made excitotoxic and sham lesions of nucleus accumbens shell in male Long–Evans rats who performed a social transmission of food preference task. In this task, observer rats revealed their original preference for one out of two food options. Afterward, they were exposed to a demonstrator rat who was fed with the observer's originally non-preferred food, and the observer's food choices were sampled again. Sham lesioned observer rats changed their food preferences following interaction with the demonstrator, specifically by increasing the intake of their originally non-preferred food type. This interaction-related change in preference was not found after nucleus accumbens shell lesions. The lesion effects on choice were not the consequence of impaired social or non-social motivation, anxiety or sensory or motor function, suggesting that they reflected a genuine deficit in social reward revaluation. These results highlight the role of nucleus accumbens shell in revaluating food rewards to match a conspecific's preferences.

KEYWORDS
decision-making, motivation, reward revaluation, social behaviour

1 | INTRODUCTION

Rats, as many social species, acquire information from peers in order to make decisions; in consequence, their food choices are based not only on individual experiences but also on conspecifics' feeding behaviour. The socially transmitted food preference (STFP) paradigm is a task that adapts this naturalistic form of social learning to the laboratory settings. In one variant of this paradigm, observer rats choose between two appetitive food items and reveal a preference for one of them. Subsequently, observers interact with conspecifics, called demonstrators, previously fed with the non-preferred food. Upon

Abbreviations: ANOVA, analysis of variance; ITI, intertrial interval; NAc, nucleus accumbens; NAcC, nucleus accumbens core; NAcSh, nucleus accumbens shell; ODI, odour discrimination index; OF, open field; PBS, phosphate-buffered saline; PI, preference index; SEM, standard error of the mean; STFP, socially transmitted food preference.

social interaction, observers have been found to increase their consumption of the food consumed by the demonstrator, thus, overwriting their endogenous food preference (Galef & Whiskin, 2008). Hence, the STFP allows exploring the behavioural and brain mechanisms of a form of socially driven change in preference.

In humans, the alignment to social opinions and preferences has been named *Conformity*, and it has been measured with a variety of stimuli such as music (Zaki et al., 2011) or facial attractiveness (Campbell-Meiklejohn et al., 2010). Several studies have identified the role of the ventral striatum in encoding agreement with the group and stimuli endorsed by others (Wu et al., 2016). In this regard, Nook and Zaki (2015) tested whether group norms shift the food preference of the subjects. They measured the subjects' food ratings before and after the group's rating feedback. The strength of the nucleus accumbens (NAc) activation during consensus between the subject and the group predicted their conformity on food preference. Moreover, group norms changed subjects' internal evaluation of the food; hence, conformity was not a result of public compliance but of a revaluation of the reward.

Revaluation of reward can be observed in non-human animals, too. For example, rats increase their food-seeking behaviour after the upvaluation, driven by a hunger state, of a previously known reward (Wassum et al., 2011). Non-social reward revaluation has been shown to depend on the integrity of NAc (Aitta-Aho et al., 2017; Katsuura & Taha, 2014), in particular NAc shell (NAcSh) subregion (Sweis et al., 2018). In addition, there is some evidence hinting at a potential involvement of NAc in social decision-making and social information processing in rodents in general (De Leonibus et al., 2006; Dölen et al., 2013; Okuyama et al., 2016; Smith et al., 2021). Finally, a recent study identified NAc as the only brain region that showed activity that was selectively correlated with socially motivated helping behaviour (Ben-Ami Bartal et al., 2021). Considering the role of NAcSh in reward revaluation and social behaviour, we asked if the NAcSh is relevant for the adaptive behaviour observed in the STFP paradigm.

To address this question, we trained rats in the STFP paradigm. We compared the strength of the post-versus-pre social interaction preference change between a group of rats with lesions of their NAcSh and sham lesioned rats. We furthermore asked if the socially transmitted change in preference is driven by the devaluation of the preferred food, the upvaluation of the non-preferred food, or both, and if this process is impaired by the NAcSh lesion. Finally, to probe the long-term stability of the post-interaction preference, we evaluated food choices a week after STFP performance. An odour discrimination test and an anxiety test were carried out to control possible confounding effects caused by the surgery.

2 | MATERIALS AND METHODS

2.1 | Subjects

Sixty male Long–Evans rats (*Janvier, France*), 48 observers and 12 demonstrators, were used for this experiment. All animals were about 10–11 weeks old and weighed between 255 and 320 g at the date of surgery. Observer rats were housed in pairs and demonstrators in groups of three until they were all housed individually. The housing room was kept at a constant temperature of $22°C \pm 2°C$ and a humidity of approximately $55\% \pm 2\%$, and animals were under an inverted 12:12 light–dark cycle. Before being moved to single housing, rats received standard laboratory rodent food (*Sniff, Germany*) and water ad libitum. During the STFP testing period, rats were food restricted to 85% of their free-feeding body weight, and food rations were given daily after finishing the experimental procedure. All rats were handled for 5 min/day for 2 days prior to the surgery and again after recovery. Six rats did not survive surgery and one was euthanized because it fulfilled standardized criteria for a humane endpoint (OECD, 2000). Three rats were not included in the analysis after applying histology exclusion criteria (see below), and further four rats were excluded because of no food consumption during testing. Consequently, 34 observer rats were included in the final analysis, 16 in the NAcSh lesioned group and 18 in the sham group. All animal procedures were conducted in accordance with the German Welfare Act and were approved by the local authority LANUV (Landesamt für Natur-, Umwelt- und Verbaucherschutz North Rhine-Westphalia, Germany).

2.2 | Surgical procedures

Rats were pseudorandomly assigned to receive either a lesion of the NAcSh or a sham surgery. Prior to surgery, rats received analgesia (5 mg/kg carprofen s.c.). Inhalation was induced with 5% isoflurane until rats lost mobility, and then, isoflurane levels were lowered to 2% to 3% for maintaining anaesthesia. Upon reaching surgical state, rats were fixed in a stereotactic frame using blunt ear bars (David Kopf Instruments, USA). The skull was exposed, two holes were drilled, and bilateral infusions were made using a .3 mm injection needle connected to a microinfusion pump via a polyethylene tubing at the following coordinates relative to bregma: AP .14 cm;

ML $\pm$ .08 cm; and DV $-.79$, $-.69$ and $-.64$ cm. Infusions were made using .5 μl of .05 M quinolinic acid (*Sigma Aldrich*) dissolved in .1 M phosphate-buffered saline (PBS) with a pH value of 7.4 for the lesioned animals or PBS for sham animals. The infusion rate was set at .5 μl/min, and the needle remained in place for 1 min allowing liquid diffusion at the injection site. Rats were left to recover for at least 1 week, receiving analgesia (5 mg/kg carprofen s.c.) during the first 2 days after surgery.

2.3 | Open field test

An open field (OF) test was conducted to assess potential differences in locomotion and anxiety between the groups. Rats were placed in the centre of a square arena (50 × 50 cm) and could freely explore it for 10 min while being recorded by a camera from above. Behavioural parameters were assessed by offline analysis using tracking software (Ethovision, Noldus Information Technology, The Netherlands). The time spent in the centre, the entrance frequency and the latency of the first entrance were analysed as measures of anxiety. Time spent in the centre of the OF is understood as a sign of low anxiety, while staying close to the walls displays higher anxiety levels (Prut & Belzung, 2003). In addition, the parameter distance moved was measured to assess potential motor abnormalities induced by the lesion.

2.4 | Odour discrimination task

To assess potential lesion-related differences in odour recognition, an odour discrimination task was conducted the day after the anxiety test in the same OF. The task consisted of a 5-min sample trial, 15-min intertrial interval (ITI) and a 5-min test trial. In the sample trial, two bowls were placed at two corners of the maze. They contained the same odour, either grape or banana-flavoured pellets (*test diet*) diluted with water (1:3 water). The bowls were covered with a lamellar grid preventing the animals from drinking the diluted flavoured pellets; hence, any discrimination between bowls was based on olfactory information only. The location and type of odour were pseudorandomized across subjects. In the test

trial, one of the two bowls contained the familiar odour from the sample trial, and the other bowl contained a novel odour. We measured the time rats spent exploring the bowl with the novel odour relative to the one with the familiar odour. The time spent smelling each bowl was manually scored from recorded videos using Solomon Coder (Solomon Coder beta 19.08.02 © András Péter).

2.5 | STFP task

The detailed experimental timeline is shown in Figure 1. Three days before the beginning of the STFP task, observers and demonstrators were housed individually and placed on food restriction. For habituation purposes, 10 grape and 10 banana-flavoured pellets were given to all rats in hanging feeders. The STFP task consists of three phases: pre-interaction testing, interaction and post-interaction testing.

2.5.1 | Pre-interaction testing

On the first day of the testing, observer rats received two weighed cups in their home cage, one containing each food type (grape and banana). The cups were located in hanging feeders and observers were allowed free access for 6 h, after which the cups were removed and weighed. The same procedure was repeated the following 2 days. On completion of pre-interaction testing, observers' individual preferences were calculated by measuring how much of each reward they consumed, quantified as the difference in cup weight before versus after the 6 h consumption period.

2.5.2 | Interaction

On the fourth day of the STFP task, observers and demonstrators were transported to a room adjacent to the interaction room. Demonstrators were fed prior to interaction with the food type that was not preferred by their assigned observers. In order to intensify the corresponding odour, the demonstrator had his back, snout and anal
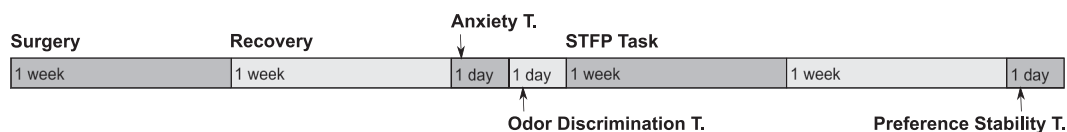

FIGURE 1 Experimental timeline

area covered with crushed pellets. The interaction took place in the OF and lasted for 20 min. The following mutually exclusive behaviours were analysed for each animal by two independent evaluators using Solomon Coder: partner exploration, genital exploration, social play, mounting, allogrooming, fighting and following.

2.5.3 | Post-interaction testing

Observer rats were placed back in their single cages immediately after the interaction and received two cups, one with each food type. As in the pre-interaction testing, cups were removed and weighed 6 h later. The preference examination was repeated the following day. Afterward, all animals were placed back in group housing.
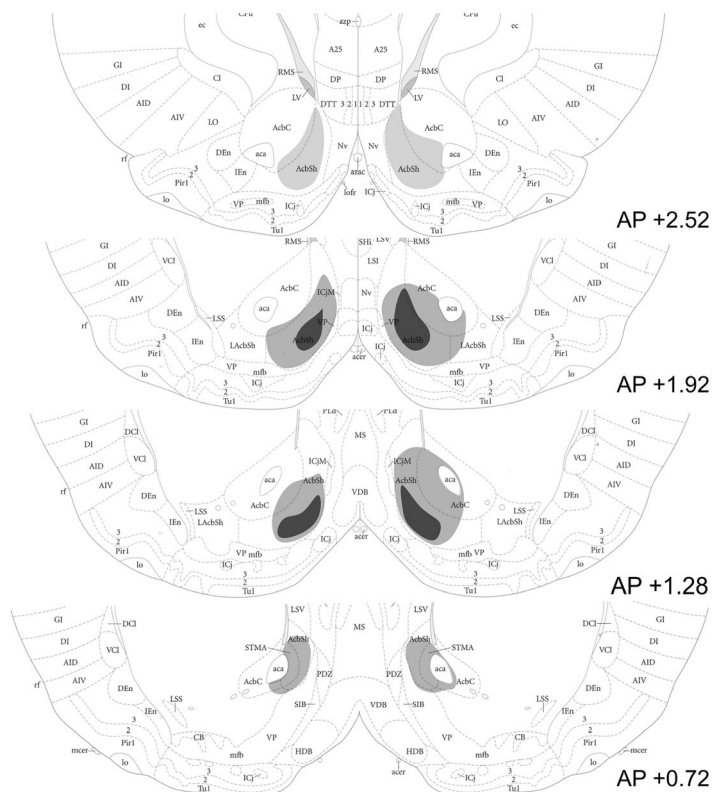
2.6 | Long-term stability of STFP

To determine the long-term stability of the socially transmitted preference, we conducted another preference test 7 days after completing the STFP task. Again, both food types were given to the observer rats and the amount eaten of each food type was measured 6 h later.

2.7 | Histology

To verify the accuracy of the lesion, rats were deeply anaesthetized with sodium pentobarbital and perfused transcardially with 4% paraformaldehyde in .1 M phosphate buffer. Brains were immediately removed and stored in the fixation solution at a temperature of 5°C. Coronal sections of the NAcSh were cut at a thickness of 50 µm using a vibratome (Leica, Germany) and stained with cresyl violet. Pictures of the NAcSh (Figure 2b) were taken with the microscope Leica DM750 at two magnifications (4× and 10×) and the camera Leica ICC50 HD. Percentage of lesioned areas was calculated using ImageJ (1.53k) software by manually outlining the area with neurotoxic damage. Exclusion criteria were unilateral or misplaced lesions. One rat in the NAcSh lesioned group was excluded due to the wrong location of the lesion, another one due to unilateral lesion and a third one due to a unilateral extension of the lesion to bordering areas.
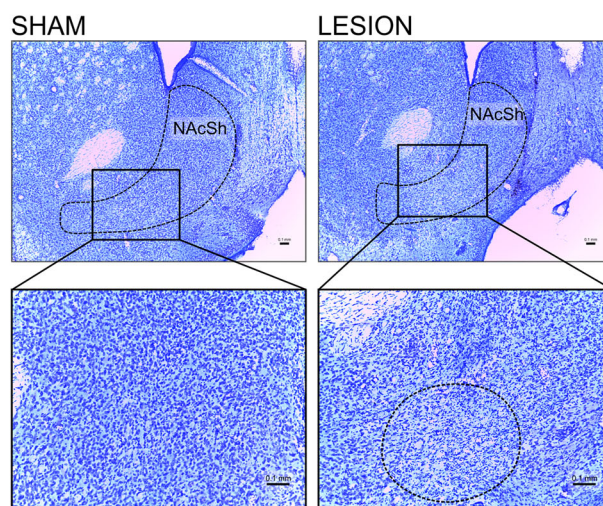
FIGURE 2 Schematic and photomicrograph representation of NacSh lesions. (a) Schematic representation of NAcSh lesion placements from anterior to posterior coordinates. The most overlapping lesions are located in the medial region of the NAcSh and some spread to the core. Light colour: maximum lesion overlap; dark colour: minimum lesion overlap. (b) An example brain slice of sham and NAcSh lesioned group. Pictures are adapted from the atlas of Paxinos and Watson (2006).

2.8 | Data analysis

We expressed the preference magnitude for one food type over another with a preference index (PI). The PI was based on the grams of each food type consumed, and it was computed separately for each day period using the following equation:

$$PI = \frac{(preferred\,(g) - nonpreferred\,(g))}{(preferred\,(g) + nonpreferred\,(g))}.$$

The data were analysed using mixed analyses of variance (ANOVAs; SPSS 27, IBM, USA; R 3.6.3; R Core Team, 2020) with two groups (sham vs. NAcSh lesion) as between-subjects factor and contact (pre-interaction vs. post-interaction) and days (Days 2–5) as within-subjects factor. Original preference (preferred vs. non-preferred) was added as a within-subjects factor to evaluate the effect of each food type on STFP performance. To evaluate the effects of the extensions of the lesions, the difference in the PI before and after the social interaction was correlated with the percentage of lesion extension (averaged between hemispheres). Statistical significance was assumed when $p < .05$. Post hoc analyses were performed with t tests. Correlations were calculated with Pearson's or Kendall's τ_b correlation coefficient as applicable. Benjamini–Hochberg correction was applied to correct for multiple comparisons.

The PI was also calculated after the long-term recall assessment, which was compared with the measurements from Day 3 (before the interaction) and Day 4 (after the interaction) to test stability. Moreover, we also identified the proportion of full preference reversals after the interaction; a full preference reversal was defined as the higher consumption of the originally non-preferred food than the originally preferred food after the interaction. The frequency of reversed preferences was compared between groups on the fourth and the fifth day of the STFP with a Fisher's exact test.

Finally, to assess the social motivation of the rats, we grouped the different interaction subtypes into two variables: the observer interaction time, which includes the subtypes where the observer had an active role (partner and genital exploration, allogrooming and following), and the mutual interaction time where the total amount of time spent interacting was aggregated (partner exploration, genital exploration, social play, mounting, allogrooming, fighting and following). Observer interaction was assessed besides mutual interaction because previous literature has shown that the role of the demonstrator during the interaction has minimum effects on the STFP task (Galef et al., 1983, 1988). To check for differences in social motivation between groups, we performed t test, or Wilcoxon tests, depending on the normality of the distribution of the respective data. Because of technical problems, social interaction data from two NAcSh lesioned rats and one sham lesioned rat were lost and, therefore, not included in the analysis.

For the odour discrimination task, an odour discrimination index (ODI) was computed from the test trial by dividing the total time spent exploring the new odour by the total time spent exploring both odours (new + familiar). We used two-sample t test to determine whether the ODI differed between sham and NAcSh lesioned groups. To analyse anxiety, a multivariate ANOVA was performed with groups as the independent variable and centre-cumulative duration, centre frequency and centre latency as dependent variables.

3 | RESULTS

3.1 | Histology

Histological assessment of lesions was performed by I. N-C. and confirmed by one additional individual (S.S.). The rats in the NAcSh lesioned group had bilaterally a greater number of apoptotic cells or tissue damage in NAcSh than the sham lesioned group. Excitotoxic damage extended rostrocaudally from +2.56 to +.72 mm AP, with average maximal extension between +1.92 and +1.28 mm anterior to bregma and between .6 and 2 mm mediolaterally as defined by Paxinos and Watson (2006). The average percentage of NAcSh lesioned was 20.64% ± 2.29%. However, there was a significant difference in the percentage of NAcSh damaged between hemispheres (Figure S1, Wilcoxon test; $z = 2.43$, $p = .015$), being larger in the left hemisphere (28.03% ± 4.68%) than in the right hemisphere (13.25% ± 2.58%). Lesions occasionally extended unilaterally into the core of the nucleus accumbens (NAcC; $n = 6$; average percentage extension of 26.7% ± 13.83%) but not into other neighbouring regions. Nevertheless, the region that was commonly lesioned in all lesioned rats was NAcSh. Some animals ($n = 8$) in the sham group had small lesions, albeit not confined to NAcC or NAcSh, and the lesions were substantially less pronounced than the ones observed in the NAcSh lesioned group and qualitatively different, that is, less evidence for apoptotic cells. The sham group lesions were probably caused by the needle insertion during surgery. Three animals were excluded from the NAcSh lesioned group following exclusion criteria. A schematic representation of the lesions together with one example image of each observer's group is shown in Figure 2.
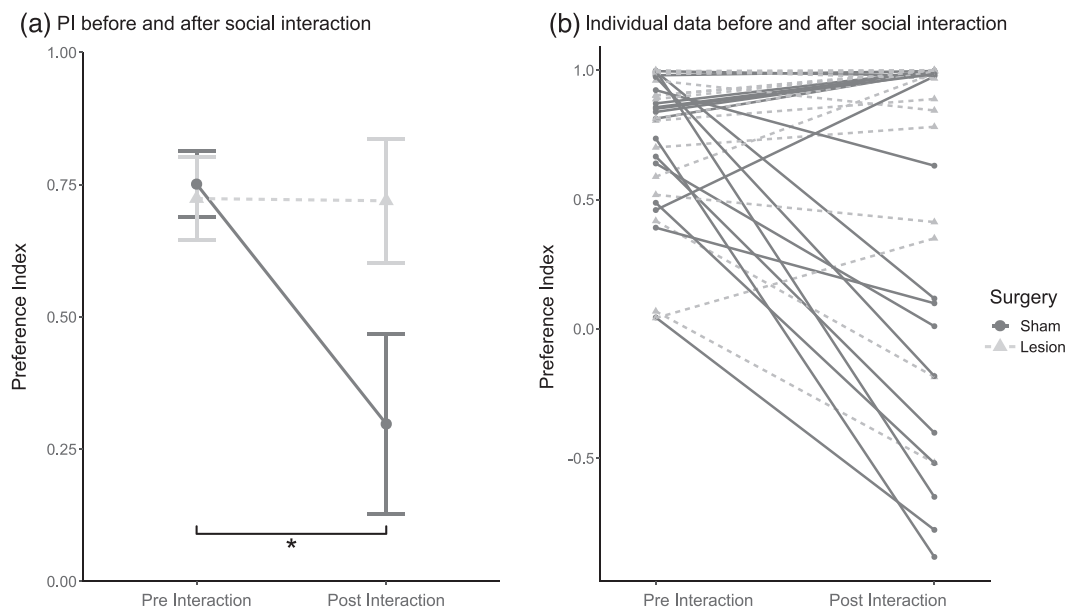
3.2 | NAcSh lesions reduce the socially induced preference change after the interaction

In order to compare preferences, we calculated the PI for each observer rat, which reflects how much more preferred than non-preferred food the rat has eaten. To test the hypothesis that the NAcSh lesions impair STFP performance, we ran a mixed ANOVA on the effects of group (sham vs. NAcSh lesion), contact (pre-interaction vs. post-interaction) and day (Days 2–5) on the PI. We found a significant simple main effect of contact ($F_{[1, 32]} = 5.955$, $p = .02$), indicating an influence of interaction on the PI. We also found a significant statistical interaction between group and contact ($F_{[1, 32]} = 6.798$, $p = .014$). Importantly, we did not find a significant interaction between contact, day and group ($F_{[1, 32]} = 1.698$, $p = .202$). Therefore, we average the PI of the days before the interaction (Days 2 and 3) and the days after the interaction (Days 4 and 5) for the following analysis and the graphical representation of the data. A post hoc analysis revealed a decreased post-interaction PI for the sham group ($t_{[17]} = 2.89$, $p = .02$), but not for the NAcSh lesioned group ($t_{[15]} = .064$, $p = .95$), suggesting that the post-interaction change in preference was less pronounced in the lesion than the sham group (Figure 3). We further analysed whether the magnitude of the change in PI was correlated with the extension of the lesion. However, this correlation did not reach significance (Kendall's test; $\tau_b = .217$; $p = .242$; Figure S2). The total amount of food eaten did not differ between groups along the STFP task ($F_{[1, 32]} = .812$, $p = .37$; food consumption data in Table S1).

The lack of PI adjustment shown by the NAcSh lesioned group could either be due to an impaired socially transmitted reward revaluation or due to a generally reduced social motivation. To control for the latter possibility, we compared the time the observers spent interacting with the demonstrators between groups. We found that observer interaction time and mutual interaction time were not different between groups (observer interaction, $t_{[22.72]} = .55$, $p = .59$; mutual interaction, $z = -.516$, $p = .606$) indicating that social motivation was unlikely reduced after NAcSh lesion.

The socially transmitted change in preference found in the STFP task may either be the consequence of the upvaluation of the originally non-preferred food type, the devaluation of the originally preferred food type or both. To address this question, and to determine whether NAcSh lesions interfered with reward upvaluation or devaluation, we ran a mixed three-way ANOVA on food consumption (the amount of food consumed) with the within-subjects factors original preference (originally preferred vs. non-preferred food), contact (pre-interaction vs. post-interaction) and the between-subjects factor group (sham vs. NAcSh lesion). Not surprisingly, we found main effects of contact ($F_{[1, 32]} = 9.912$, $p = .004$)

(a) PI before and after social interaction

(b) Individual data before and after social interaction

Surgery
—●— Sham
--▲-- Lesion

FIGURE 3 Effects of the NAcSh lesion on preference index (PI). Dotted, light grey lines and triangle symbols represent data from the lesioned group, solid, dark grey lines and circle symbols represent data from the sham group. (a) The PI expresses the difference between preferred and non-preferred food eaten relative to the total food eaten before and after the interaction with the demonstrator (mean ± standard error of the mean, SEM). The PI is significantly decreased in sham lesioned, but not in NAcSh lesioned rats, after social interaction. (b) Change in the PI after social interaction for each individual rat. *$p < .05$.

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and original preference ($F_{[1,\ 32]} = 58.245$, $p < .001$) on food consumption. Importantly, we also found a significant three-way statistical interaction effect ($F_{[1,\ 32]} = 5.824$, $p = .022$) on food consumption. Breaking down this three-way statistical interaction (Figure 4; individual values in Figure S3), post hoc tests revealed no significant differences in preferred food consumption pre-interaction versus post-interaction in either group of rats (sham, $t_{[17]} = 1.98$, $p = .128$; lesion, $t_{[15]} = -.92$, $p = .495$). By contrast, we did find a significant increase in the amount of non-preferred food consumed pre-interaction versus post-interaction in the sham group ($t_{[17]} = -3.02$, $p = .032$). This increase in amount of non-preferred food consumed was not found in the lesioned animals ($t_{[15]} = -.47$, $p = .644$). This pattern of results suggests that the STFP effect is mainly driven by a socially transmitted upvaluation of the originally non-preferred food type, and to a lesser, statistically insignificant extent, by a devaluation of the originally preferred reward. NAcSh lesions interfered with social upvaluation of reward.

In summary, we found evidence for a socially transmitted change in food preference in the sham group, but not in the NAcSh lesioned group. This effect was mainly driven by the upvaluation of the originally non-preferred food type in a NAcSh-dependent way. These lesion effects on STFP are unlikely due to reduced reinforcer sensitivity, decision-making capacity or general social motivation.

3.3 | NAcSh lesions reduce the frequency of preference reversals

To further characterize the strength of the demonstrators' influence on the observers' food preferences, we compared the proportion of sham versus NAcSh lesioned rats reversing their preferences after interaction (i.e., the preference is considered reversed if a rat consumed more originally non-preferred food than originally preferred food after the interaction); 38.9% (7/18) of the sham lesioned rats reversed their preference completely, while only 6.25% (1/16) of the NAcSh lesioned rats did it on the fifth day (Fisher's exact test; $p = .04$ two sided; Figure 5). Even if not significant, this tendency appeared already on the fourth day, following interaction (Fisher's exact test; $p = .12$ two sided).

3.4 | Post-interaction food preferences are stable across time

To evaluate the stability of the food preference in each group, we measured the observers' food consumption a week after finishing the STFP task. We ran a mixed ANOVA and found a significant simple main effect of time (Day 3 pre-interaction vs. Day 4 post-interaction vs. Day 15 post-interaction) on the PI ($F_{[2,\ 64]} = 5.473$, $p = .006$) and a statistically significant interaction between group and time ($F_{[2,\ 64]} = 3.227$, $p = .046$). A
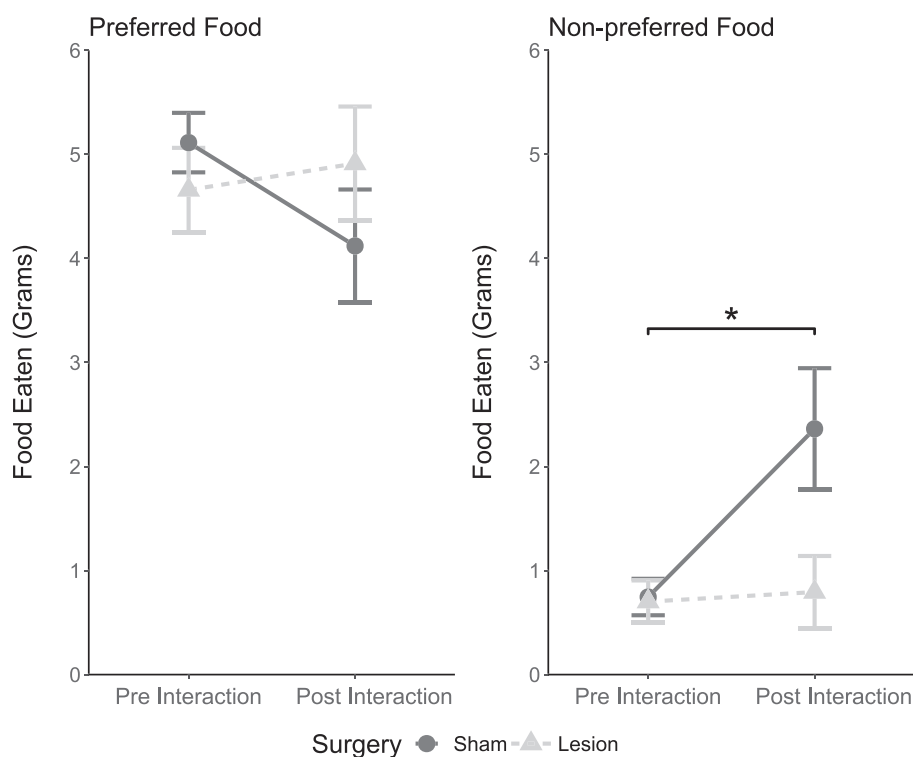
FIGURE 4 Preference change of originally preferred and non-preferred food types. Mean (±SEM) of the originally preferred and non-preferred food consumption in grams before and after the social interaction for each group. The consumption of the preferred food type did not significantly change after interaction in either group. By contrast, sham rats significantly increased their consumption of the non-preferred food type after interaction, which was not observed in NAcSh lesioned rats. *$p < .05$.
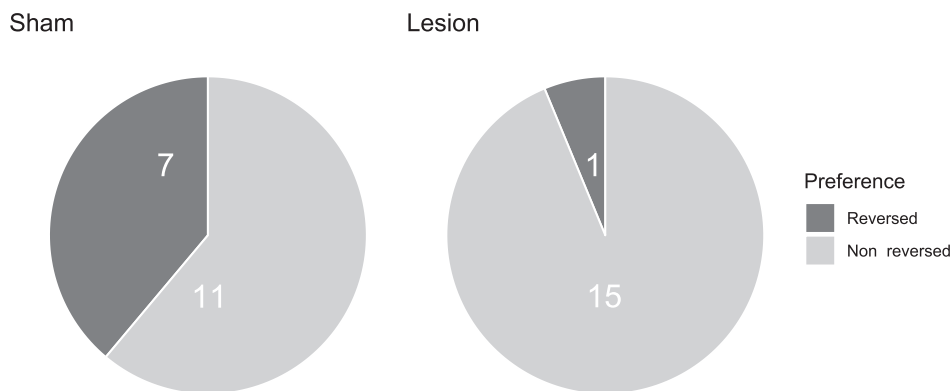
Sham   Lesion

FIGURE 5 Preference reversal. Frequency of full preference reversals on the fifth day (1 day after social interaction). Seven of 18 sham lesioned rats fully reversed their preference, that is, they ate more originally non-preferred than preferred food after the interaction, while only 1 of the 16 NAcSh lesioned rats fully reversed its preference. The frequency of reversed preference was significantly higher in the sham group than in the NAcSh lesioned group.

post hoc analysis revealed that, not surprisingly, the PI of that sham group decreased after the interaction (Day 3 vs. Day 4, $t_{[17]} = 3.23$, $p = .015$). Interestingly, in sham rats, the post-interaction PI on Day 15 was still significantly different from the pre-interaction PI (Day 3 vs. Day 15, $t_{[17]} = 3.2$, $p = .015$), and their preference remained nearly unchanged over time following the interaction (Day 4 vs. Day 15, $t_{[17]} = -.188$, $p = .853$; Figure 6; individual values in Figure S4). Therefore, we conclude that the influence of the demonstrators on the PI of the sham group was long-lasting. By contrast, there were no differences between any of the days in the NAcSh lesioned group (Day 3 vs. Day 4, $t_{[15]} = .273$, $p = .8$; Day 3 vs. Day 15, $t_{[15]} = 1.07$, $p = .6$; Day 4 vs. Day 15, $t_{[15]} = .639$, $p = .8$), revealing temporal stability of food preference and, once again, insensitivity to social influence.

3.5 | No lesion effects on odour discrimination

The STFP task requires the rats to be able to distinguish between odours because they have to associate the odour of the food eaten by the demonstrator with its breath. We evaluated whether both sham and NAcSh lesioned rats can discriminate between odours, manifested by exploring the novel odour for a longer time than the familiar one in the odour discrimination task. During the test trial, the ODI for both groups together was higher than chance ($t_{[33]} = 5.722$, $p \le .001$). In addition, there were no significant differences in the ODI between groups ($t_{[31.8]} = -.682$, $p = .5$; Figure 7e). Thus, both groups were able to recognize odours. Therefore, lesion-related differences in STFP performance were unlikely due to deficits in odour recognition.
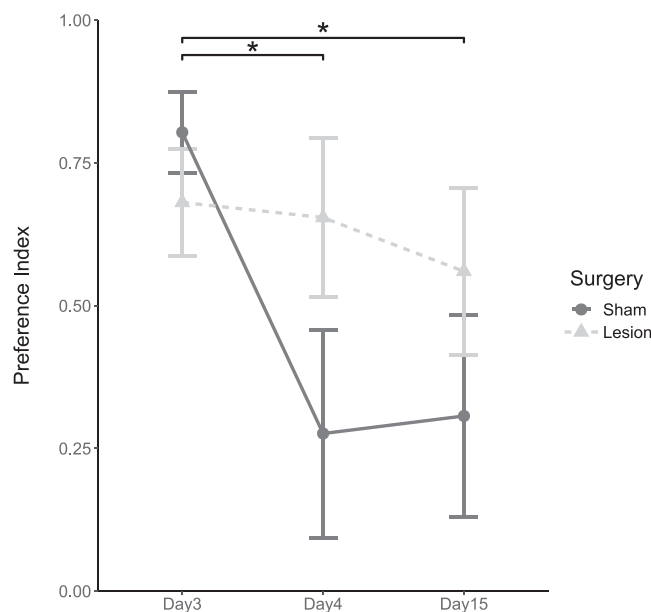

FIGURE 6 Long-term stability of food preferences. The mean of the preference index (±SEM) on Day 3 reflects the original preference pre-interaction, on Day 4 the preference after interaction and on Day 15 the preference 11 days after interaction. *$p < .05$.

3.6 | The NAcSh lesioned group is more anxious than the sham group

Anxiety can modulate sociability and food consumption (Lopes et al., 2012; Shah & Treit, 2003). Therefore, we compared anxiety levels between NAcSh and sham lesioned rats, measured by the time spent in the centre of the test arena, the frequency of entering the arena centre and the latency of the first entrance (see Section 2). The multivariate ANOVA revealed a main effect of group on
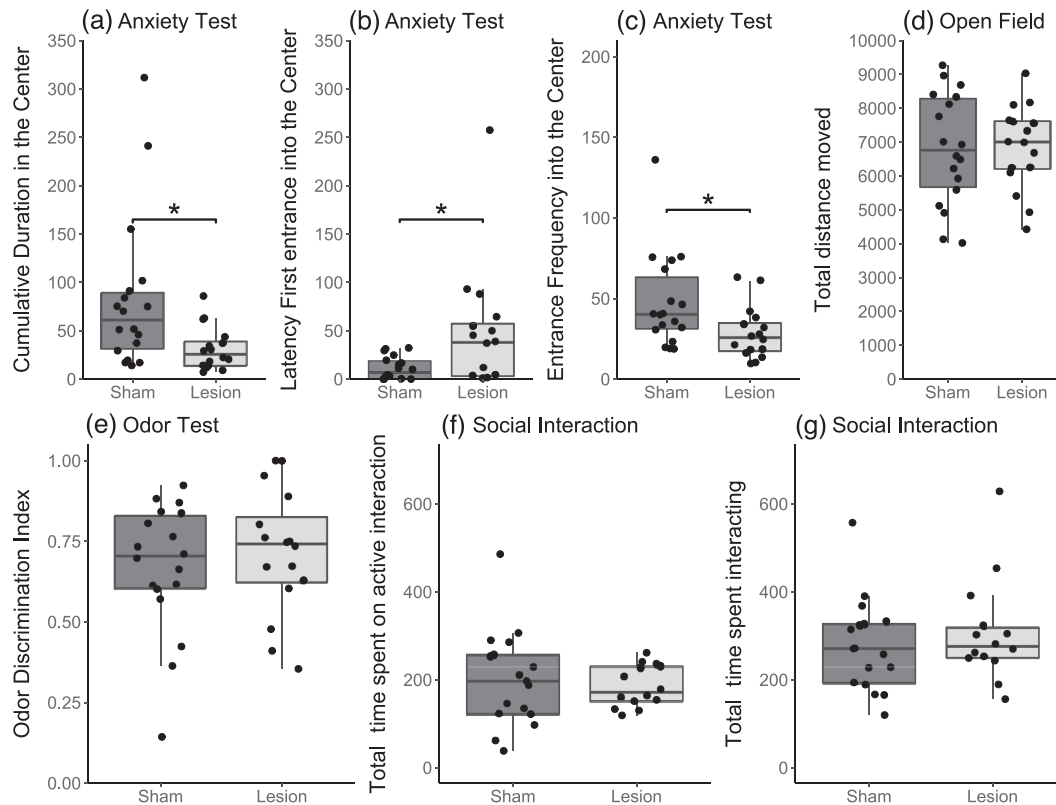
FIGURE 7 Control measures. (a–c) Effect of the NAcSh lesions on anxiety levels. (a) Significant differences in the cumulative duration (s) spent in the centre of the open field (OF) between groups. (b) Significant differences in the latency (s) of the first entrance to the centre of the OF between groups. (c) Significant difference in the frequency of the entrances to the centre of the OF between groups. The three measurements reveal higher anxiety levels for the NAcSh lesioned group than the sham group. (d) Total distance moved. The distance moved (cm) in the OF was not affected by NAcSh lesions. (e) Effect of the NAcSh on the odour discrimination index. Relative time spent investigating the new odour with respect to the total time spent investigating both odours (new and familiar). There were no significant differences between groups in their capacity to differentiate odours. (f,g) Effect of the NAcSh on social interaction during STFP. (f) The total time (s) spent interacting with the demonstrators initiated by the observers was not affected by NAcSh lesions. (g) The total time (s) spent on social interaction independent on the initiator was not affected by NAcSh lesions. *$p < .05$. Points represent individual values.

anxiety ($F_{[3, 30]} = 3.394$, $p = .03$). Post hoc analyses revealed that NAcSh lesioned animals had higher levels of anxiety than sham lesioned rats in each of the three anxiety measurements (centre-cumulative duration, $t_{[32]} = 2.61$, $p = .035$; centre latency first, $t_{[32]} = 2.41$, $p = .035$; and centre frequency, $t_{[32]} = -2.21$, $p = .042$; Figure 7a–c). We also measured locomotion (distance moved) in the OF (Figure 7d) but found no significant differences between groups ($t_{[32]} = -.77$, $p = .939$).

Considering these results, each rat's individual centre-cumulative duration as a measure of anxiety was added as a covariate to the mixed ANOVA we used to analyse the lesion effects on STFP behaviour. Adding anxiety as a covariate did not change the results of the ANOVA reported above on the effects of lesion (sham vs. NAcSh lesion) and contact (pre-interaction vs. post-interaction) on PI (contact and group statistical interaction, $F_{[1, 31]} = 5.168$, $p = .03$). The variable anxiety did

not significantly explain either the performance differences between groups caused by social interaction in the STFP task (contact and centre-cumulative duration statistical interaction, $F_{[1, 31]} = .00014$, $p = .991$). Thus, we conclude that the lesion effects on STFP performance were unlikely due to differences in anxiety levels between sham and NAcSh lesioned rats.

4 | DISCUSSION

Rats modify their food preference in order to conform to a conspecific's preference. In the present study, we hypothesized that the integrity of NAcSh is necessary for adjusting own food preference to match the preferences of a conspecific. To test this hypothesis, we trained NAcSh and sham lesioned rats in a STFP task. Sham lesioned rats changed their food preference after

interacting with a conspecific who was fed with the originally non-preferred food. By contrast, the NAcSh lesioned rats stuck by their original preference, showing no change in food choices after social interaction. We furthermore found that, in sham rats, the STFP effect was driven primarily by an increased demand for the originally non-preferred food item after social interaction and to a lesser extent by a decreased demand for the originally preferred item. NAcSh lesioned rats did neither change their consumption of the originally preferred, nor the non-preferred food post-interaction. In a significant proportion of the sham lesioned rats, the influence of the demonstrator was strong enough to fully reverse their preference, while almost none of the NAcSh lesioned rats showed full preference reversals. We additionally found a long-lasting influence of social interaction on food preference in the sham lesioned group, replicating previous results (Galef & Whiskin, 2003), while, once again, no social long-term effect on food preference was found in the NAcSh lesioned animals. Overall, we provide evidence that NAcSh lesions impair the rats' ability to modify their own food preference to match the preference of a conspecific.

What could be the putative function of NAcSh in STFP? The effects of lesions on STFPs may be the result of a deficit in reward revaluation, that is, in using social information to update reward value representations. Alternatively, it is equally plausible to explain our findings as a general deficit in motivation or decision-making. However, we consider the latter explanation unlikely because the NAcSh lesioned rats showed consistent and stable preferences for one reward over the other, and there was no difference in reward intake and social interaction time between groups. Thus, we have no evidence to assume social or non-social anhedonia in our NAcSh lesioned rats. We, therefore, conclude that the selective deficit in socially transmitted reward revaluation is the more plausible interpretation of our lesion results.

Another explanation of the lesion effects on STFPs is a putative change in anxiety. In line with previous literature (Gebara et al., 2021; Martínez et al., 2002), we report that NAcSh lesioned rats had higher novelty-induced anxiety levels when exposed to an unfamiliar environment than sham lesioned rats. However, we found no differences in social interaction or food consumption between sham and lesioned rats, and adding anxiety as a covariate did not change our results. Hence, the group difference in novelty-induced anxiety did not seem to generalize or transfer to other behavioural domains. Therefore, it is unlikely that differences in anxiety levels between groups explain the lesion effects on STFP performance.

The NAcSh lesion effects on STFP performance could also be due to an impairment in cognitive flexibility instead of the result of an interference with a genuinely social-cognitive process. However, it has been shown that the integrity of the NAcSh is not necessary for reversal learning, a common task used to evaluate cognitive flexibility (Castañé et al., 2010). If anything, the full or partial disruption of the NAcSh seems to facilitate, rather than impair, cognitive flexibility across different paradigms (Gal et al., 2005; Jongen-Rêlo et al., 2002; Milton et al., 2021; Pothuizen et al., 2005; Sala-Bayo et al., 2020; but see Ding et al., 2014). In addition, the experimental designs used to evaluate cognitive flexibility were all based on variations of reinforcement learning paradigms in which animals learn the incentive value of initially neutral stimuli. However, reinforcement learning is probably less relevant for the behavioural change shown in the current study, which presumably does not involve learning or modifying the value of initially neutral stimuli (Galef & Durlach, 1993). In a similar vein, a NAcSh lesion-induced proneness for habit formation might also explain the lesioned rats' tendency to continue choosing the originally preferred reward after social interaction. Habit formation describes the acquisition of action values, independent of the actions' outcomes. However, because the action to obtain one reward or another was nearly identical in our STFP task, lesion-related differences in action values are unlikely to manifest in differences in food choices. In addition, the existing literature points toward the dorsal striatum as the main region relevant for habitual (stimulus–response) behaviour while the ventral striatum, which contains the NAcSh, is more important for goal-directed (action-outcome) behaviours (Belin et al., 2009; Devan et al., 2011; Everitt & Robbins, 2013; O'Tousa & Grahame, 2014). Thus, although we cannot entirely rule out that a lesion-related change in cognitive flexibility or habit formation might account for our findings, we consider these explanations less parsimonious than the social reward revaluation hypothesis presented above.

Thus, in conclusion, we argue that neither social nor non-social anhedonia, novelty-induced anxiety, impairments in cognitive flexibility, non-specific sensory (olfaction) or motor deficits can account for the lesion effects on STFPs. We, therefore, maintain that the most likely explanation is that our findings are the consequence of NAcSh lesion-induced social reward revaluation deficit.

Abundant literature on the STFP paradigm has tested several variations of the original task design to delimit its interpretation. A crucial finding was that the acquisition of the STFP requires exposing the observer rat to the odour together with either a breathing rat or a toy rat moistened with carbon disulphide—a chemical present in rats' breath (Galef et al., 1988). By contrast, the mere exposure to the scent of food alone (Choleris et al., 2011; Galef et al., 1985)

or covering a toy demonstrator does not enhance the preference for such food (Galef & Stein, 1985). Therefore, the change in preference cannot be explained by a recency effect, where the last odour smelled determines the consumption preference. Interestingly, the demonstrator's health state is not relevant (Galef et al., 1983), as observers acquire food preferences even from anaesthetized demonstrators. Although this result seems counterintuitive, it ratifies the breath as the most informative cue among the characteristics of the demonstrator.

The STFP phenomenon is very robust: It is independent of the motivational state of the observer (food deprived or ad libitum), the form of ingesta (liquid or solid), the age of both rats, familiarity and strain when it is assessed unidirectionally (Galef et al., 1984; but see Figueroa et al., 2020). Nevertheless, variability increases when both rats influence each other simultaneously in a more ecological setting. While the major impact on preference is degraded when rats forage in pairs, they make use of the information transmitted by the other in a different manner depending on the context, the partner and individual characteristics (Damphousse et al., 2019). Galef and Whiskin (2004) also showed that the transfer of preferences between conspecifics is stronger in a stable environment than in a variable one. These data indicate that rats, far from acting automatically to the information transmitted by a conspecific, integrate it into a complex decision-making process.

The design of this study comes with some limitations that should be considered. Both groups underwent surgery and were isolated for seven consecutive days in order to conduct the STFP and another 3 days to evaluate the long-term stability of the transferred preference. However, our results are comparable with STFP literature, where those stressors are not present (Galef & Stein, 1985; Galef & Whiskin, 2008). Nevertheless, demonstrators were used for consecutive interactions with different observers (to reduce the number of animals used) understanding that either habituation or sensitization could occur. As the transmission of information seems to be a passive process not dependent on demonstrators' characteristics, as discussed above (Galef et al., 1988), the impact of such order should be limited. Moreover, the order of the observers paired with the demonstrators was randomized between groups.

The NAcSh is a hotspot for many reward-related processes, including hedonic pleasure (Castro & Berridge, 2014) and motivated behaviour (Ito & Hayen, 2011). Berridge and Robinson (1998) proposed that NAc is necessary to attribute incentive salience to reward-associated cues and actions, and their neural representations, boosting their attractiveness and, thus, driving motivation. Several studies have provided evidence supporting their hypothesis (Peciña & Berridge, 2013; Saddoris et al., 2015, 2017; Salamone et al., 1994, 2003; Sclafani et al., 2011; Wyvell & Berridge, 2000). Concretely, NAcSh mediates motivational and affective valence along a rostrocaudal gradient (Reynolds & Berridge, 2002, 2003). Accordingly, NAcSh is a key player in choice revaluation during economic decision-making in mice (Sweis et al., 2018), and in modulating food preferences in a non-social operant conditioning task in rats (Jang et al., 2017; Katsuura & Taha, 2014). NAcSh seems to play a similar role in social tasks, too: Ben-Ami Bartal et al. (2021) have identified the NAcSh as a neural hub for promoting prosocial motivated helping behaviours in rats. We expand on this body of literature by implying NAcSh in socially motivated reward choice behaviour. However, associative processes, valuation and motivation are dissociable mechanisms (Wassum et al., 2009) that our experimental design cannot distinguish. Thus, a conservative interpretation of our results understands the NAcSh as an essential region within the neural circuit encoding the processes involved in the STFP performance and does not assume the localization of the mentioned processes exclusively in the NAcSh. Considering so, we argue that NAcSh integrity is necessary for incorporating social information during the revaluation of food rewards. Consequently, it is plausible that the revaluation deficit seen in the NAcSh lesioned rats is the consequence of their inability to process the incentive salience of the non-preferred food after being associated with a social stimulus, i.e., here, the social interaction. Therefore, we interpret that the change in consumption in the sham group is driven by an upvaluation of the non-preferred food after its salience is increased by the association with the social stimulus.

The neural underpinning of the STFP task is partly known. The orbitofrontal cortex is necessary for STFP acquisition (Ross et al., 2005; but see Smith et al., 2010) as well as the prelimbic cortex (Boix-Trelis et al., 2007; Gold et al., 2011; Portero-Tresserra et al., 2013), the parafascicular nucleus (Quiroz-Padilla et al., 2006) and the basolateral amygdala (Carballo-Márquez et al., 2009; Wang et al., 2006). Indeed, olfactory regions as the anterior olfactory nucleus and the olfactory bulb are crucial for this task acquisition (Wang et al., 2020). Moreover, the perirhinal cortex is required for STFP long-term memory (Feinberg et al., 2011). Still, the most studied memory-related region has been the hippocampus with contradictory results (Alvarez et al., 2001; Burton et al., 2000; Clark et al., 2002; Feinberg et al., 2011; Winocur et al., 2001; but see Thapa et al., 2014). Although the role of the rats' NAcSh in STFP has not been investigated before, our results are in line with a previous study on mice where the activation of the

piriform cortex to the mPFC network targeting the NAc was essential for STFP acquisition and expression (Loureiro et al., 2019). Our demonstration of the role of the NAcSh in this paradigm complements our knowledge of the neural underpinning of the STFP task in rats.

In conclusion, this current study provides evidence that the integrity of rat NAcSh is necessary for STFP. The stability of the original food preference after social interaction observed in the NAcSh lesioned group is not due to a general decrease in social motivation or feeding, nor in locomotion deficits, odour discrimination impairments, nor anxiety. Future research is needed to disentangle the mechanistic processes underlying the STFP and to evaluate which neurotransmitters are involved in the present task and how the NAcSh is connected to the other implicated regions. Our results suggest that NAcSh lesions result in a deficit in socially transmitted reward revaluation and provide novel information about the role of the NAcSh in social behaviour.

CONFLICT OF INTEREST

The authors declare no competing financial interests.

PEER REVIEW

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DATA AVAILABILITY STATEMENT

Raw data supporting the findings presented in the study is openly available in OSF at https://osf.io/p3emb/.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.