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Research report

Orbital prefrontal cortex and guidance of instrumental behaviour in rats under reversal conditions

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Abstract

The orbital prefrontal cortex (OPFC) is suggested to be part of a circuitry mediating the perception of reward and the initiation of adaptive behavioural responses. In the present study, we investigated in rats changes of goal-directed behaviour after bilateral OPFC-lesions by *N*-methyl-D-aspartate (NMDA) in more detail. A reaction time (RT) task was used which is sensitive to subtle changes in discriminative guidance of instrumental behaviour by the anticipated reward magnitudes. The task demands conditioned lever release triggered by an imperative stimulus. The upcoming reward magnitude (five or one food pellet) for each trial was randomly chosen and signalled in advance by distinct instructive stimuli. In trained rats, RTs of instrumental responses were determined by the two distinct stimulus–reward magnitude contingencies, i.e. RTs were shorter to the instructive stimulus predictive of the higher reward magnitude. Results show that lesions of the OPFC did not impair discriminative guidance of behavioural responses according to preoperatively acquired stimulus–reward magnitude contingencies. However, guidance of instrumental behaviour was altered in lesioned rats after a reversal of the stimulus–reward magnitude contingencies. The data add further support to the hypothesis that the rat OPFC is not involved in retrieval of acquired stimulus–reward magnitude contingencies but in integration of incentive information to guide behaviour after a reversal of stimulus–reward contingencies.

Keywords: Reward; Reward magnitude; Goal-directed action; Reaction time; Stimulus–reward learning; Instrumental learning; Orbitofrontal

1. Introduction

The orbital prefrontal cortex (OPFC) has been widely suggested as part of a circuitry through which information on the incentive value of stimuli influences the selection and execution of reward-directed behavioural responses [5,13,19,21]. This hypothesis is based on findings that monkeys and humans with damage to OPFC exhibit behavioural impairments after changes of stimulus–reward contingencies [7,8,16,20,22]. Furthermore, electrophysiological data indicate that the acquired incentive value of cues is encoded in OPFC neurons [15,18,29,32]. In addition, firing to discriminative cues in OPFC neurons does not correlate with reinforcer identity, but reflects the incentive value of the reinforcer [24,31]. Besides, cue-selective firing in OPFC is altered markedly after changes in cue–outcome contingencies [24,25,30]. As changes in cue-selective firing induced by cue–outcome alterations are time-locked to changes in choice behaviour, neuronal activity in OPFC might represent the conjunction of the acquired incentive value of the cues with the use of that information to guide performance [23,24,26].

The role of the OPFC in control of goal-directed behaviour has been explored primarily in monkeys and humans. The few rat studies available so far demonstrate subtle behavioural impairments after inactivation of the rat OPFC which were strongly task-dependent and in part inconsistent across different studies. For example, rats with OPFC-lesions were impaired after reversal in an olfactory discrimination task [27], while other studies showed that rats with OPFC-lesions were not affected during the first, but during a second serial reversal in a discrimination task [9]. On the other hand, rats with transient OPFC-inactivation were not impaired after reversal of stimulus–reward contingencies in a two-lever task [6].

The present study was designed to examine in more detail behavioural changes in rats with OPFC-lesions. To this end, a reaction time (RT) task was used which is sensitive to subtle changes in discriminative guidance of instrumental behaviour by anticipated reward magnitudes [4,11,12].

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In this task, RTs of instrumental responses were determined by distinct stimulus–reward magnitude contingencies. We tested whether OPFC-lesions impaired (1) discriminative guidance of instrumental behaviour according to preoperatively acquired stimulus–reward magnitude contingencies, and (2) behavioural adaptation to a postoperative reversal of stimulus–reward magnitude contingencies.

2. Materials and methods

Experiments were performed according to the German Law on Animal Protection and approved by the proper authorities in Stuttgart, Germany.

2.1. Subjects

Thirty-three male Sprague–Dawley rats (Charles-River, Sulzfeld, Germany) were maintained in a temperature- and humidity-controlled room on a 12 h light:12 h dark schedule (lights on 07:00–19:00 h) with testing in the light phase. All rats were given ad libitum access to water. Standard laboratory maintenance chow (Altromin, Lage, Germany) was restricted to 12 g per animal per day. On days with behavioural tests, rats received 6–7 g food reward (45 mg pellets, Bioserv, Frenchtown, USA) in the testing apparatus. On these days, the amount of standard laboratory chow was adapted in order to keep body weights nearly constant. Rats weighed 200–225 g on arrival, 250–310 g at the time of surgery and 260–330 g at the end of the experiment.

2.2. Surgery

For stereotaxic surgery, rats were anaesthetized with sodium pentobarbital (50 mg/kg, i.p.) (Sigma–Aldrich, Taufkirchen, Germany) following pretreatment with atropine sulphate (0.05 mg/kg, i.p.) (Sigma–Aldrich, Taufkirchen, Germany) and secured in a Kopf stereotaxic apparatus (Kopf Instruments, Tujunga, USA). Standard stereotaxic methods were used for bilateral microinjections of *N*-methyl-D-aspartate (NMDA) (Tocris Cookson Ltd., Bristol, UK) at the following coordinates: 4.0 mm anterior to bregma, 1.8 and 3.0 mm lateral to midline, and 4.6 mm ventral from the skull surface [17]. A second set of bilateral injections was made at 3.0 mm anterior to bregma, 2.8 and 3.6 mm lateral to midline, and 5.6 mm ventral from the skull surface. At each of the four sites per hemisphere, NMDA (20 mg/ml) (OPFC-lesioned group, $n = 11$) or the Krebs'–Ringer's solution phosphate vehicle (sham-lesioned group, $n = 11$) was delivered in a volume of 0.1 μl over a 1 min interval. The injector was left in situ for a further 3 min to allow for diffusion. Each rat was given at least 7 days to recover from surgery before postoperative training was started. The lesion protocol was similar to the one described elsewhere [10]. One group of rats (un-operated group, $n = 11$) did not underwent surgery.

2.3. Apparatus

Four operant test chambers (24 cm × 21 cm × 30 cm) (Med Associates, St. Albans, USA) were placed in separate sound attenuating cubicles with fans providing a constant low level of background noise. Each chamber was supplied with a retractable lever, a food dispenser with receptacle on the right hand side of the retractable lever and two stimulus lights, one above the retractable lever (providing the imperative stimulus) and one above the food receptacle (providing the instructive stimulus). The experiments were controlled online (SmartControl®-Interfaces; Med Associates, St. Albans, USA) by a computer system (MedPC-Software; Med Associates, St. Albans, USA).

2.4. Reaction time task

A simple RT task [11,12] was used which demands conditioned lever release with instructive stimuli indicating the reward magnitude to be obtained after a subsequent imperative stimulus.

Rats had to press the lever and to wait for the imperative stimulus after a foreperiod of 0.3 s. The imperative stimulus signalled to release the lever quickly and to respond to the food receptacle in which the food pellets were delivered (45 mg pellets, Bioserv, Frenchtown, USA). On each correct trial, the rats received one or five food pellets. The number of pellets for each trial was randomly determined in advance and signalled to the rats by two distinct brightness levels of the instructive stimulus light. The instructive stimulus light was turned on at the beginning of each trial before lever press and remained present until delivery of food reward. To check for equal perception of the two different brightness levels of the instructive stimulus light, for 50% of the rats, the bright stimulus was associated with delivery of five pellets and the dim stimulus was associated with delivery of one pellet. For the other 50% of the rats, the opposite pattern was used.

RTs defined as latency from the onset of the imperative stimulus to lever release were recorded with an accuracy of 10 ms. For a correct trial, rats had to release the lever within 1.5 s after presentation of the imperative stimulus. Responses before onset of the imperative stimulus were defined as "early" responses, responses with RTs longer than 1.5 s were defined as "late" responses. A daily individual session lasted approximately 10 min and demanded 50 correct trials, i.e. 25 correct trials for each reward magnitude (one and five pellets). However, the initial training sessions lasted up to about 30 min until the criterion was reached. All rats were trained in one daily session on 5 days per week during the complete experimental period. A schematic representation of the order of trial events is given in Fig. 1.

2.5. Experimental procedure

2.5.1. Habituation

On the first day, subjects were habituated to the operant chamber with access to food pellets placed into the food

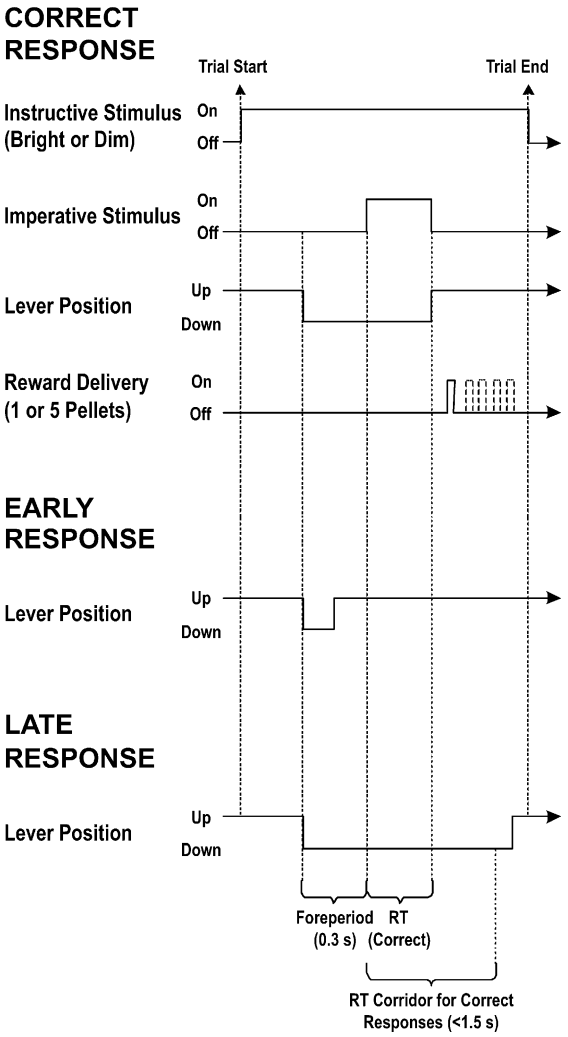

Fig. 1. Schematic representation of the order of trial events. At the beginning of a trial, the instructive stimulus light was turned on at one of two brightness levels which were associated with different reward magnitudes (one or five pellets). Thereafter, the rat pressed the lever spontaneously. After a foreperiod of 0.3 s, the imperative stimulus light was presented signalling the rat to release the lever in order to get the food reward. Responses with reaction time (RT) <1.5 s were considered as being correct and were rewarded as indicated by the instructive stimulus (top). Early responses (before onset of the imperative stimulus) (middle) or late responses (RT > 1.5 s) (bottom) caused the trial to be repeated with the identical foreperiod and reward magnitude.

receptacle. The following days, a habituation program with a FR-1 schedule commenced until a criterion of 20 consecutive lever responses was attained.

2.5.2. Preoperative sessions

Rats were trained in the RT task for 20 sessions. Thereafter, the correct response rate was at least 70%, i.e. rats needed at maximum 71 trials to attain the necessary 50 correct responses. In addition, mean RTs of all responses of a session with an expected low reward magnitude were significantly longer than those with an expected high reward magnitude, i.e. responses were guided by the expected reward magnitude. Afterwards, rats were subjected to surgery.

2.5.3. Retrieval sessions

After at least 7 days of recovery, retrieval of preoperatively learned stimulus–reward magnitude contingencies was tested for 25 sessions. After retrieval, correct response rate was at least 70% and mean RTs of all responses of a session with an expected low reward magnitude were significantly longer than those with an expected high reward magnitude in all treatment groups.

2.5.4. Reversal sessions

Subsequently, acquisition of reversed stimulus–reward magnitude contingencies was tested for 60 sessions, i.e. rats had to acquire that the stimulus formerly predicting high reward magnitude was under reversal conditions associated with low reward magnitude (and vice versa).

2.6. Data analysis

Results showed equal perception of the two different brightness levels of the instructive stimulus light, i.e. all rats discriminated stimulus–reward magnitude contingencies irrespective of the brightness–reward magnitude relationship. For example, in the last retrieval block, RTs of responses of the subgroup of OPFC-lesioned rats with the dim stimulus indicating low reward magnitude (578 ± 18 ms) were significantly longer than RTs of responses with the bright stimulus indicating the high reward magnitude (527 ± 15 ms) ($F_{(1,86)} = 4.01$, $P = 0.0483$). For the other subgroup of OPFC-lesioned rats, RTs of responses with the bright stimulus indicating the low reward magnitude (617 ± 18 ms) were significantly longer than RTs of responses with the dim stimulus indicating the high reward magnitude (545 ± 16 ms) ($F_{(1,86)} = 10.00$, $P = 0.0022$). Furthermore, RTs for each reward magnitude level of both subgroups did not significantly differ ($F_{(1,86)} = 2.79$, $P = 0.0986$). Therefore, performance and RT data obtained with both stimulus–reward magnitude contingencies were pooled. For analysis, data were grouped into blocks of five sessions.

Accuracy of task performance was determined by using (1) the mean total number of trials per session (± standard error of the mean, S.E.M.), and (2) the correct response rate, i.e. the percent means of correct responses from the total number of trials per session (±S.E.M.). Two-way analyses of variance (ANOVAs) of each experimental period (preoperative, retrieval, reversal) were conducted with treatment groups as between factor and blocks as within (repeated measures) factor followed by planned contrasts.

The calculations of RT performance were conducted with RT data from correct responses (RT < 1.5 s). Geometric RT means instead of arithmetic means of responses with the expected high and low reward magnitude, respectively, were calculated for the individual rat for each session as the geometric mean is less affected by extreme values than is the

arithmetic mean [14]. Overall RT means of responses with the expected high and low reward magnitude, respectively, represent the arithmetic average of the geometric means of individual rats [3]. Preoperatively as well as after retrieval, RTs of responses with an expected low reward magnitude were significantly longer than those with an expected high reward magnitude. Calculated RT differences (±S.E.M.) reflecting RT guidance by reward magnitude expectancy based on instructive stimuli [11] were further analysed by ANOVAs followed by planned contrasts. A calculated "positive" difference between RTs with expected low versus high reward magnitudes indicates intact determination of instrumental responses by the expected reward magnitudes.

Statistical computations were carried out with the STATISTICA ('99, StatSoft Inc., Hamburg, Germany) statistical package. The level of statistical significance (α-level) was set at $P < 0.05$.

2.7. Histology

On completion of behavioural testing, rats were euthanized with Ethrane® (Abbott, Wiesbaden, Germany) and transcardially perfused with 350 ml 0.02% heparin sodium salt solution (Gibco BRL, Grand Island, NY, USA), followed by 400 ml 4% formalin (Schuchardt, Hohenbrunn, Germany). Brains were removed, post-fixed in 4% formalin for 20 h, and stored in 30% glucose. Brain sections (30 μm) were cut with a cryostat (Reichert & Jung, Heidelberg, Germany), mounted on coated slides and stained with cresyl violet. Sham- and OPFC-lesions were analysed [17].

3. Results

3.1. Histological results

Infusion of NMDA resulted in extensive neuronal loss and gliosis in ventrolateral and lateral orbital regions. Only rats with OPFC-lesions encompassing at least 50% of ventrolateral and lateral orbital regions were included in data analysis. Two rats were excluded from the OPFC-lesioned group because their lesions encompassed less than 50% of ventrolateral and lateral orbital regions. On average, lesions of the rats included in data analysis encompassed 80% of OPFC bilaterally, ranging from 50 to 100%. The largest lesions reached to the medial orbital area and included some minor damage to claustrum and frontal, parietal and agranular insular cortex. No relationship between any behavioural measure and the extent of the encroachment of the lesions on adjacent structures was observed in any animal used for data analysis. Therefore, no animal was excluded because of large lesions including some damage to other areas. The approximate extent and placement of OPFC-lesions of all rats included in data analysis is depicted in Fig. 2. In sham-lesioned rats, no mechanical damage caused by the four injections per hemisphere was observed.

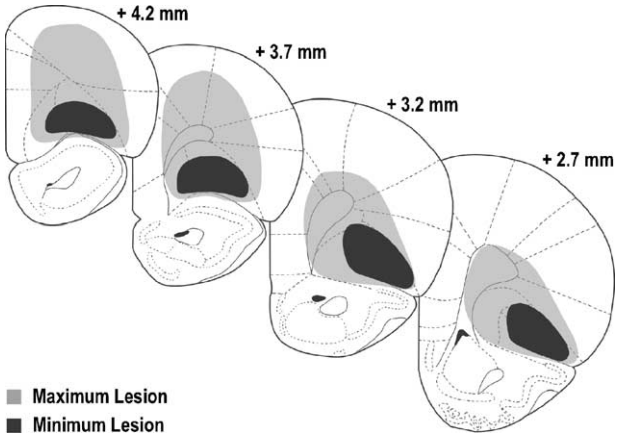

Fig. 2. Schematics showing the area of orbital prefrontal cortex damage. The schematics depict the approximate extent and placement of the orbital prefrontal cortex lesions for all rats used for data analysis. Black and shaded regions, respectively, represent the minimum and maximum extent of cell loss across animals. Plates are adaptations from the atlas of Paxinos and Watson [17]. Numbers beside each plate correspond to millimetres anterior to bregma.

3.2. Performance in preoperative and retrieval sessions

3.2.1. Correct response rate

In all preoperative and retrieval blocks, correct response rate ranged from 83 to 89%. A two-way ANOVA on correct response rates with treatment groups as between factor and preoperative and retrieval blocks as within (repeated measures) factor indicated significant differences neither between treatment groups nor between blocks.

3.2.2. RT performance

Mean RTs were significantly longer with expectancy of a low reward magnitude resulting in positive RT differences in all treatment groups in the last retrieval block (Fig. 3). RT performance in OPFC-lesioned, sham-lesioned and un-operated groups did not differ: a two-way ANOVA on RT differences with treatment groups as between factor and preoperative and retrieval blocks as within (repeated measures) factor revealed significant differences neither between the three treatment groups nor between preoperative and retrieval blocks (Fig. 4).

3.3. Performance in reversal sessions

3.3.1. Correct response rate

Reversal of stimulus–reward magnitude contingencies did not alter correct response rate compared to preceding retrieval sessions. In addition, there were no significant differences between treatment groups.

3.3.2. RT performance

In the last retrieval block before reversal testing, RT differences were positive, i.e. RTs were longer with the stimulus indicating low reward magnitude. Fig. 5 depicts

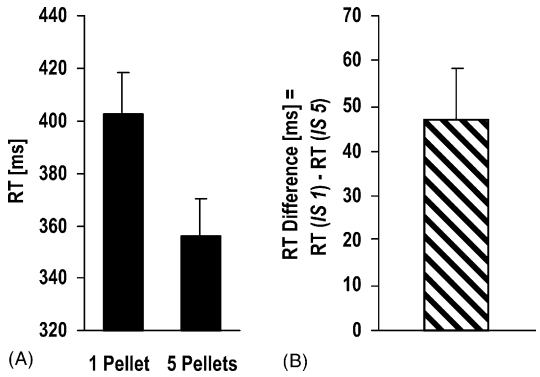

Fig. 3. Effect of the number of expected pellets on reaction times (RTs) in the last retrieval block in un-operated rats ($n = 11$, $n = 50$ correct responses per animal). (A) Mean RTs (±S.E.M.) were significantly determined by the number of expected pellets: RTs of responses with an expected low reward magnitude were significantly longer than those with an expected high reward magnitude. (B) The calculated "positive" RT difference between RT with an expected low vs. high reward magnitude reflects an intact determination of behavioural responses by the two stimulus–reward magnitude contingencies. RT (*IS 1*): RT of responses with the instructive stimulus indicating one pellet; RT (*IS 5*): RT of responses with the instructive stimulus indicating five pellets.

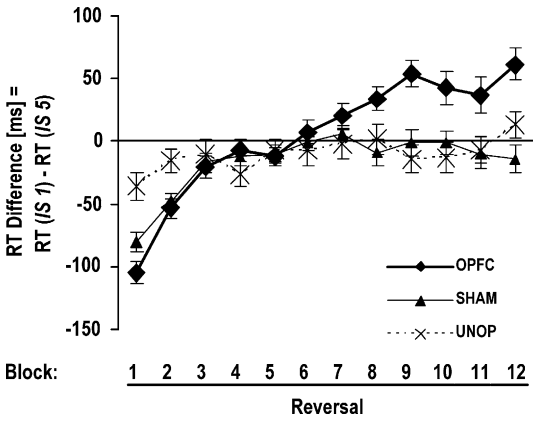

Fig. 5. Effect of OPFC-lesion on reaction time (RT) differences (±S.E.M.) during reversal testing. In the first reversal blocks, RT differences were negative because RTs were significantly shorter with the instructive stimulus which originally indicated high but under reversal conditions low reward magnitude. During the following blocks, RT differences became only gradually less negative in un-operated (UNOP) and sham-lesioned (SHAM) groups and positive in OPFC-lesioned (OPFC) group. RT (*IS 1*): RT of responses with the instructive stimulus indicating one pellet; RT (*IS 5*): RT of responses with the instructive stimulus indicating five pellets.

the changes of RT differences during reversal testing. In the first blocks of reversal testing, RT differences were negative indicating that RTs were longer to the stimulus predictive of high reward magnitude. Thus, animals responded to the stimuli according to their prior significance. Over the next blocks of reversal testing, RT differences became less negative in sham-lesioned and un-operated groups and positive in OPFC-lesioned group. A two-way ANOVA on RT differences with treatment groups as between factor and reversal blocks as within (repeated measures) factor revealed that there was a significant treatment effect ($F_{(2,152)} = 4.83$, $P < 0.01$), a significant block effect ($F_{(11,1672)} = 25.99$, $P < 0.001$) and a significant treatment × block interaction effect ($F_{(22,1672)} = 5.76$, $P < 0.001$). Further comparisons with planned contrasts indicated that the OPFC-lesioned group was significantly different from the sham-lesioned and un-operated groups in the 1st (un-operated group: $F_{(1,152)} = 26.74$, $P < 0.001$), 2nd (un-operated group: $F_{(1,152)} = 11.82$, $P < 0.001$), 8th (un-operated group: $F_{(1,152)} = 4.22$, $P < 0.05$; sham-lesioned group: $F_{(1,152)} = 7.77$, $P < 0.01$), 9th (un-operated group: $F_{(1,152)} = 20.79$, $P < 0.001$; sham-lesioned group: $F_{(1,152)} = 13.47$, $P < 0.001$), 10th (un-operated group: $F_{(1,152)} = 11.35$, $P < 0.001$; sham-lesioned group: $F_{(1,152)} = 7.10$, $P < 0.01$), 11th (un-operated group: $F_{(1,152)} = 6.32$, $P < 0.05$; sham-lesioned group: $F_{(1,152)} = 7.44$, $P < 0.01$) and 12th (un-operated group: $F_{(1,152)} = 8.78$, $P < 0.01$; sham-lesioned group: $F_{(1,152)} = 21.94$, $P < 0.001$) reversal blocks. In the first reversal block, RT difference was less negative in sham-lesioned than in OPFC-lesioned rats; contrast test indicated that this effect missed statistical significance ($F_{(1,152)} = 3.39$, $P = 0.06$).

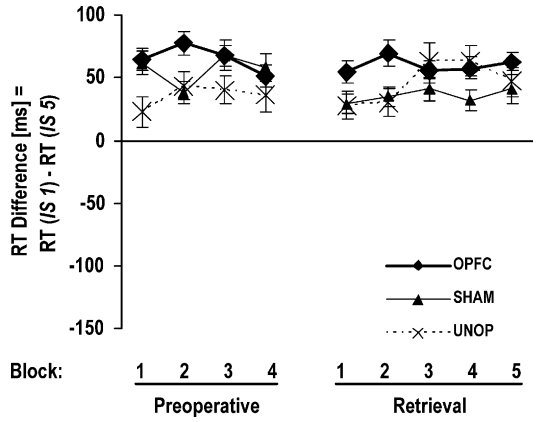

Fig. 4. Effect of OPFC-lesion on reaction time (RT) differences (±S.E.M.) during postoperative retrieval testing. In all pre- and postoperative blocks, RT differences were positive indicating intact stimulus–reward magnitude discrimination, i.e. RTs were longer with the stimulus associated with low reward magnitude. In all postoperative retrieval blocks, OPFC-lesioned (OPFC), sham-lesioned (SHAM) and un-operated (UNOP) rats showed comparable levels of RT performance. RT (*IS 1*): RT of responses with the instructive stimulus indicating one pellet; RT (*IS 5*): RT of responses with the instructive stimulus indicating five pellets.

4. Discussion

The present study reveals that OPFC-lesions did not impair discriminative guidance of instrumental behaviour according to preoperatively acquired stimulus–reward magnitude contingencies. However, OPFC-lesions altered guidance of instrumental behaviour if stimulus–reward magnitude contingencies were reversed.

4.1. NMDA-lesions of the OPFC

Lesions were generally large and—on average—encompassed 80% of OPFC. The extent determined here is in line with the size of OPFC-lesions by NMDA detected in previous studies [9,10,27]. To ensure that the stereotaxic procedure per se (four injections per hemisphere) did not induce unspecific damage causing behavioural impairments, an un-operated group was included additionally. Performance of un-operated and sham-lesioned rats did not differ significantly in any variable measured in postoperative tests. In addition, inspection of cresyl violet stained slices from sham-lesioned rats depicted no signs of mechanical damage in OPFC. Thus, it is unlikely that the stereotaxic procedure per se produced OPFC-injury resulting in behavioural alterations.

4.2. Performance in preoperative sessions

Two variables with different sensitivity were used to characterize task performance: correct response rate and RT performance. The correct response rate was defined as the percent means of correct responses from the total number of responses (including early and late responses) to reach the 50 correct trials demanded per session. Correct response rate ranged from 83 to 89% indicating a high level of instrumental performance which exceeded those in comparable tasks [4,11,12]. Furthermore, preoperative RTs of responses with an expected low reward magnitude were significantly longer than those with an expected high reward magnitude resulting in a "positive" RT difference. Apparently, the predictive information provided by the instructive stimulus produced reward magnitude expectancies accounting for RT difference. Therefore, RT difference is a sensitive measure to characterize discriminative guidance of instrumental responses by stimulus–reward magnitude contingencies. The preoperative "positive" RT difference of approx. +50 ms corresponds to that determined in similar tasks [4,11,12].

4.3. Effects of OPFC-lesion performance in retrieval sessions

OPFC-lesions did not affect correct response rate postoperatively suggesting intact retrieval of the task without sensorimotor deficits. Likewise, RT performance was not altered by OPFC-lesions. Already in the first retrieval block, all groups, including OPFC-lesioned group, showed RT differences as positive as in the last preoperative block reflecting intact guidance of instrumental behaviour according to the anticipated reward magnitudes. Thus, OPFC does not seem to play a fundamental role in retrieval of preoperatively acquired stimulus–reward magnitude contingencies. These data correspond to recent findings in OPFC-lesioned rats which were unimpaired in acquiring go/no-go odour discrimination problems when cue–outcome relationships remained unchanged [27].

4.4. Effects of OPFC-lesion on performance in reversal sessions

During reversal of stimulus–reward magnitude contingencies, correct response rate remained unchanged in all groups compared to preceding retrieval sessions suggesting that instrumental responding is reward-directed in OPFC-lesioned, sham-lesioned and un-operated rats. However, in the first reversal blocks, RT differences were negative in all groups. Thus, cues continued to be interpreted according to their prior incentive significance. Similarly, sham-lesioned rats stayed with their previous response strategy in a comparable nine-hole box task in the initial reversal block [4]. Remarkably, in the first reversal block, RT differences of OPFC-lesioned rats were significantly more negative compared to un-operated rats. Likewise, RT differences of OPFC-lesioned rats were markedly less negative compared to sham-lesioned rats, though this effect missed statistical significance ($P = 0.06$). Thus, during early stages of reversal learning, damage to OPFC produced a stronger perseveration of RT performance according to the originally acquired stimulus–reward magnitude contingencies. Likewise, OPFC-lesions affected the initial reversal of an established response pattern in an odour-guided go/no-go discrimination task [27]. These findings in rats correspond to the general notion that humans and monkeys with OPFC-damage exhibit impairments after changes of stimulus–reward contingencies [7,8,16,20,22]. However, other studies [9] using an odour-guided go/no-go discrimination task detected no impairment after OPFC-lesions in rats during the first, but during a second serial reversal. Furthermore, rats with transient OPFC-inactivation showed intact reversal learning in a two-lever discrimination task [6]. Together, these studies suggest that the contribution of the OPFC in initial reversal learning critically depends on the type of reversal task used. Further support for a role of rat OPFC in reversal learning is provided by recent electrophysiological findings in rats. After reversal of stimulus–reward contingencies, correlated firing increased in OPFC indicating that the original associations were maintained within the OPFC while acquiring new stimulus–reward associations. This type of encoding has been suggested to facilitate comparisons of original and reversed stimulus–reward contingencies permitting faster behavioural adaptation in controls. In contrast, OPFC-lesioned rats show perseverative behaviour as the original encoding is more difficult to alter in the absence of OPFC [25,27].

In later blocks of reversal testing, RT differences became gradually less negative in sham-lesioned and un-operated groups and positive in OPFC-lesioned group, i.e. sham-lesioned and un-operated rats did not acquire reversal of stimulus–reward magnitude contingencies within 60 sessions, whereas OPFC-lesioned rats did. It is unlikely that the behaviour of sham-lesioned and un-operated rats reflects chance effects as both sham-lesioned and un-operated rats performed very similar. Thus, procedural

and task-inherent reasons might account for this effect. The fact that rats underwent intensive training for 45 sessions with the original stimulus–reward magnitude contingencies might account for their slow reversal learning. Indeed, reversal learning in tasks as used here might depend on the number of acquisition sessions since in a similar RT task control rats did not reach the level of reward magnitude discrimination acquired in 21 preceding retrieval sessions after 20 reversal sessions [4]. By contrast, in a simple visuospatial discrimination task, sham-lesioned and un-operated rats reached the level of reward magnitude discrimination acquired in six sessions already after six reversal sessions [2]. It seems that the OPFC-lesioned rats acquired reversal of stimulus–reward magnitude contingencies faster than sham-lesioned and un-operated rats in the task used here. This was surprising as in early stages of reversal learning OPFC lesions hampered reversal learning. Similarly to the present study, initial impairments of reversal learning declined in OPFC-lesioned rats and, after serial reversals, they performed significantly better than sham-lesioned rats [27]. In that study, the poor performance of control rats was attributed to trace representations of the originally acquired stimulus–reward contingencies in the OPFC which might interfere with new encoding across multiple reversals. Likewise, interference might be one possibility to account for the slower reversal learning of sham-lesioned and un-operated rats in later stages of reversal learning of the present study. The improvement of the OPFC-lesioned rats in later reversals [27] was interpreted as the emergence of a non-OPFC-dependent strategy for solving reversals which is less susceptible to interference than processes supporting reversal learning in intact rats. Furthermore, it was suggested in that study that prefrontal functions might be subsumed by other structures with practice and that these systems might operate in parallel with OPFC to some extent. Parallel processing systems which subsume OPFC functions in later stages of reversal learning might also account for the faster reversal learning of OPFC-lesioned rats in the present study. However, this notion is speculative and needs further experimental support. Furthermore, this view is limited given the methodological differences in both studies. Nevertheless, together these findings render the idea that an intact OPFC might hamper reversal learning in later stages, perhaps due to interference with original stimulus–reward magnitude contingencies.

4.5. The role of the rat OPFC: functional implications

The OPFC plays a key role within the circuitry through which information on the incentive significance of stimuli influences the selection and execution of reward-directed behaviour. In particular, the OPFC has been implicated to play an important role in adapting behavioural responses to altered incentive information in monkeys and humans [1,7,8,16,20,22]. Using a RT task highly sensitive to changes of behavioural guidance by the anticipated value of actions, the present data provide further support to the concept that the OPFC in rats is not involved in retrieval of acquired stimulus–reward magnitude contingencies but in adaptation of instrumental behaviour to changes in the incentive value of environmental stimuli [28].

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