Repetitive transcranial magnetic stimulation over the right dorsolateral prefrontal cortex affects strategic decision-making

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Although decision-making is typically seen as a rational process, emotions play a role in tasks that include unfairness. Recently, activation in the right dorsolateral prefrontal cortex during offers experienced as unfair in the Ultimatum Game was suggested to subserve goal maintenance in this task. This is restricted to correlational evidence, however, and it remains unclear whether the dorsolateral prefrontal cortex is crucial for strategic decision-making. The present study used repetitive transcranial magnetic stimulation in order to investigate the causal role of the dorsolateral prefrontal cortex in strategic decision-making in the Ultimatum Game. The results showed that repetitive transcranial magnetic stimulation over the right dorsolateral prefrontal cortex resulted in an altered decision-making strategy compared with sham stimulation. We conclude that the dorsolateral prefrontal cortex is causally implicated in strategic decision-making in healthy human study participants. *NeuroReport* 16:1849–1852 © 2005 Lippincott Williams & Wilkins.

Keywords: decision-making, dorsolateral prefrontal cortex, goal-directed behavior, human, repetitive transcranial magnetic stimulation, Ultimatum Game, unfairness

Introduction

Human economic decision-making is typically seen as a rational, cognitive process. Recent research, however, demonstrates that in strategic decision-making tasks, which include fairness and unfairness, emotional experiences of unfairness may play an important role [1]. One of the games often used to measure strategic decision-making in humans is the Ultimatum Game [2]. In the Ultimatum Game, a proposer offers a fair or unfair division of a sum of money to a responder. The responder decides to accept or reject this offer, ending the game. If the responder accepts the offer, the amount of money is split as agreed. If the responder rejects it, however, neither player receives anything. As the offers by the proposer are fixed, participants in the role of the responder would be expected to go for the maximum utility (i.e. accepting all offers). This is typically not the case, however, and responders tend to reject unfair offers [3].

The neural basis of performance in the Ultimatum Game was recently studied using functional magnetic resonance imaging [4]. An important brain area activated during unfair offers in the Ultimatum Game was the right dorsolateral prefrontal cortex (DLPFC), which was suggested to subserve cognitive control or goal maintenance in the task [4]. Goal-directed behavior requires information as to whether actions were successful in obtaining outcomes, such as rewards. People with damage to the prefrontal cortex, for instance, are characterized by problems in goal-directed behavior and in decision-making [5]. Furthermore, animal studies reported that the DLPFC couples the information of rewards to actions and controls behavior [6]. Indeed, the DLPFC has been associated with optimizing decision-making in monkeys; that is, the DLPFC may guide behavior on the basis of prior choices and outcomes [7]. Thereby, the DLPFC seems to be a convergence zone for a broad range of information and, consequently, is able to guide behavior.

In the present study, we investigate the previous suggestion that the right DLPFC is involved in goal maintenance in the Ultimatum Game [4]. To investigate a possible causal role of the DLPFC in this regard, we used repetitive transcranial magnetic stimulation (rTMS). rTMS delivers short magnetic pulses that penetrate the skull and disrupt neural processing in a noninvasive, reversible way [8]. We hypothesized that the right DLPFC is crucial for determining the strategy of rejecting unfair offers, and therefore rTMS of the DLPFC will interfere with the chosen strategy, or even shift this strategy towards more acceptance. More specifically, as the normal pattern in the Ultimatum Game is to reject unfair offers, the decision to reject an unfair offer would normally be made faster than the decision to accept the unfair offer. Our hypothesis is that after rTMS of the right DLPFC this normal pattern is changed. That is, it would take more time to reject an unfair offer and might even result in more acceptances of unfair offers after rTMS.

Participants and methods

Study participants

Seven college students (two men, five women) participated in the study (age range: 19–31 years, mean age: 24 years, SD: 4.3 years) and were paid for their participation. All participants were right-handed, except for one who was ambidextrous. Participants were screened for contraindications to TMS, neurological and medical problems. The local ethics committee approved the study (Declaration of Helsinki) and all participants provided written, informed consent after the procedure had been fully explained.

Transcranial magnetic stimulation protocol

Two conditions were contrasted, rTMS versus sham stimulation over the right DLPFC, each followed by one of two parallel versions of the Ultimatum Game. For both the rTMS and sham condition we used a MagStim Rapid magnetic stimulator (MagStim Co., Whitland, Wales) with a figure-of-eight magnetic coil with a diameter of 70 mm for each loop. Sham stimulation was accomplished using a Magstim placebo coil, which has an appearance identical to that of the real coil, and also delivers the characteristic 'click' sound. The order of both the conditions, real TMS or sham, and the two Ultimatum Games was alternated over participants. Minimum time interval between TMS and sham was 30 min, to prevent carry-over effects [9,10]. The right DLPFC site of stimulation was targeted at F4 using the electroencephalogram 10–20 coordination system according to the guidelines of previous studies [11–13]. Participants wore a head-cap during the whole experiment. The coil was placed tangential to the surface of the skull.

In the TMS condition, participants were stimulated with 1 Hz TMS during 12 min over the DLPFC, marked at the head-cap, at 45% intensity of the apparatus. This slow-frequency rTMS block was preceded with a priming block of 5 min with 6 Hz at 25% intensity of the apparatus, to prolong and intensify the depressant effect [14]. The above-mentioned parameters have been applied in earlier studies of cognitive TMS [15] and have been shown to affect brain metabolism [16]. All stimulation parameters were in accordance with safety guidelines for rTMS [17].

Ultimatum Game

Both parallel versions of the Ultimatum Game consisted of 32 trials, in which participants were subsequently presented with 16 male and 16 female proposers. Participants always played the role of the responder. In both versions of the Ultimatum Game, the money was split eight times according to the ratio 5:5 (fair) and 7:3, 8:2 and 9:1 (unfair). Participants were presented with a picture of their proposer, after which the proposal was presented and participants could respond by button press to accept or reject the offer (see Fig. 1). Participants were asked to respond as fast as possible to the offer. The different offers were assigned in a random order. Participants were paid 10% of the total amount that was earned (i.e. accepted offers) in the Ultimatum Game.

Statistical analyses

Reaction times (ms) and acceptance rates (%) were analyzed across individual trials using multilevel analysis of variance (which takes nonindependence within participants into account), as implemented in SPSS (version 11.5, SPSS Inc., Chicago, Illinois, USA). TMS condition (rTMS or Sham) was included as a fixed effect, whereas participants were regarded as correlated random effects. Behavioral responses were included as dependent variables. P values were set at 0.05, two tailed.

Results

In the analyses, we focused on the unfair offers, which is where we predicted effects of rTMS over the right DLPFC. With regard to reaction times, there was a significant effect of decision (accept or reject), $t=-2.26$, $P=0.03$ and of TMS (rTMS versus sham), $t=-4.20$, $P=0.00003$. Furthermore, there was a significant interaction between decision and TMS, $t=3.28$, $P=0.001$ (see Fig. 2). When we included only accepted trials in the analysis, there was no significant effect of rTMS ($t=0.62$, $P=0.54$), whereas when only rejected trials were selected, there was a significant effect of rTMS on reaction times ($t=-5.61$, $P<0.0001$). Furthermore, there was

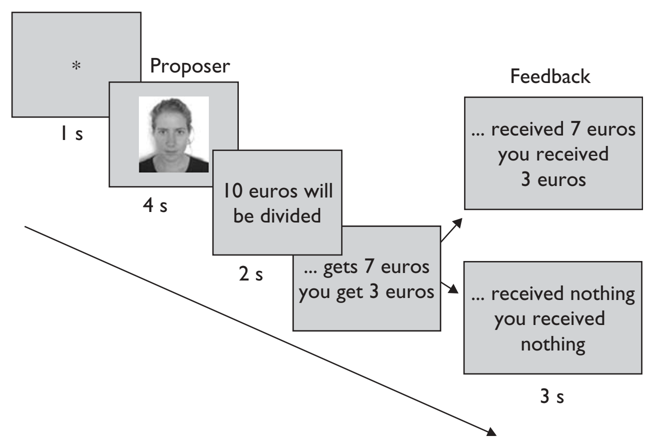

Fig. 1 A single round in the Ultimatum Game.

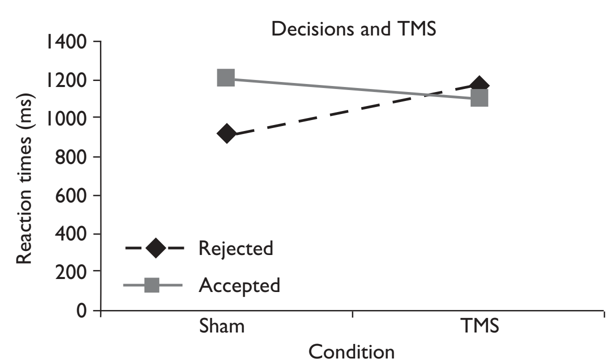

Fig. 2 Reaction times for subsequently accepted and rejected unfair offers computed for transcranial magnetic stimulation (TMS) and sham conditions separately.

a trend to accept more offers after rTMS than after sham, $t=-1.89$, $P=0.059$.

The behavioral results replicated the characteristic pattern that has been documented for responders in the Ultimatum Game: that is, all fair offers were accepted, whereas half of the unfair offers were rejected. The mean reaction time of decision-making in fair offers was 983.9 ms (SD 553 ms) for TMS and 933.4 ms (SD 352 ms) in the sham condition. The acceptance rates of unfair offers decreased as these offers became less fair. After rTMS 48.2% of unfair offers were accepted and after sham 42.3% of unfair offers were accepted. The mean reaction time of decision-making was 1141.5 ms (SD 535 ms) for TMS and 1036.5 ms (SD 442 ms) in the sham condition.

Discussion

Using rTMS, we observed a critical involvement of the right DLPFC in strategic decision-making. In the Ultimatum Game, people are confronted with fair and unfair divisions of money and individuals typically adopt a strategy of rejecting very unfair offers even though this reduces their financial earnings. Indeed, our behavioral results showed that all fair offers were accepted, but acceptance rates decreased as offers became less fair, replicating the well documented patterns of acceptance in the Ultimatum Game [2,4,18–20]. After rTMS over the right DLPFC, however, this pattern was changed, with longer reaction times for rejecting unfair offers, and a trend towards more acceptances of unfair offers.

Given the shorter reaction times and the observation that rejection of very unfair offers is more common than acceptance, rejecting unfair offers might be considered as the 'default' reaction. If the DLPFC guides goal-directed behavior by optimizing decision strategy on the basis of prior choices, neural interference by rTMS must cause behavioral interference with the default strategy; that is, choosing the rejection of unfair offers. This is exactly what we observed, as reaction times for rejection of unfair offers were prolonged after rTMS of the DLPFC. This strongly suggests a causal role for the right DLPFC in strategic decision-making. These findings are an extension of Barraclough *et al.* [7], who reported a role of the DLPFC in optimizing decision-making in monkeys. Moreover, Hadland *et al.* [21] demonstrated with rTMS that the DLPFC is important in deciding on different responses. In addition, an interference of rTMS over the DLPFC has been observed during decision-making in a spatial working memory task [12]. Future research should further elaborate on our findings by studying the causal role of the left and right DLPFC in different decision-making paradigms with TMS.

The rejection of such a great proportion of unfair offers (more than 50%) in the Ultimatum Game suggests that motives other than maximizing financial gain play a prominent role. Notably, from a social utility viewpoint, it has been suggested that the rejection of unfair offers might be more optimal than accepting these offers, as rejecting unfair offers may bolster one's position in the social hierarchy. Not receiving a small amount of money may be worth the sacrifice, to punish the persons who proposed the offer [22]. This effect also holds in single-shot encounters such as our version of the Ultimatum Game, which suggests that this is a rather intuitive mechanism that is not based on elaborate conscious reflection alone. Indeed, input from emotional systems may be of major importance, as shown by the correlation of insula activation with subsequent rejections in the Ultimatum Game [4].

Although this study supports the causal role of the right DLPFC in strategic decision-making, a limitation is that TMS was applied to the right hemisphere only. Future studies should incorporate a more complex experimental design including TMS over the right and left hemispheres and the inclusion of different cognitive measures. This design would allow conclusions regarding specificity of the right DLPFC in decision-making and the influence of other functions that are associated with the DLPFC. For instance, the DLPFC is also associated with attention and perception–action integration. We cannot rule out that these processes were affected by rTMS as well. If these processes were affected by rTMS, however, we would expect to find an overall reduction of attention or perception–action integration. In contrast, we observed a specific effect of TMS on decision-making; that is, a slowing of decision-making in reaction to unfair offers but not to fair offers.

A related issue concerns the precision of rTMS and its influence on other brain regions. Although we did not confirm the position of the DLPFC for each participant using magnetic resonance imaging scans and a neuronavigator, our procedure of targeting the F4 position of the 10–20 electroencephalogram coordination system has been frequently used in previous research and has been shown to correspond to the right DLPFC [11–13]. Moreover, the DLPFC is a relatively large area, and as TMS affects approximately 1–2 cm in diameter [23] it is safe to assume that the DLPFC was successfully targeted.

A second point refers to the influence of TMS on other brain areas connected to the DLPFC. rTMS over the DLPFC might affect other, connected regions as well, which has also been suggested with regard to the beneficial effects of rTMS over the right DLPFC on depression [24]. Future research should focus on the possible effects of rTMS over the DLPFC on a more widespread network subserving decision-making.

Conclusion

The present findings extend neuroimaging studies of the role of the DLPFC in decision-making. Whereas these studies are based on correlational rather than causal evidence, the present findings of an altered decision-making strategy after rTMS suggest a causal role of the right DLPFC in strategic decision-making.

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