Exp Brain Res (2006)
DOI 10.1007/s00221-006-0457-z

RESEARCH NOTE

**Demis Basso · Martin Lotze · Lavinia Vitale
Florinda Ferreri · Patrizia Bisiacchi
Marta Olivetti Belardinelli · Paolo Maria Rossini
Niels Birbaumer**

The role of prefrontal cortex in visuo-spatial planning: a repetitive TMS study

Received: 1 June 2005 / Accepted: 16 March 2006

Abstract The visuo-spatial planning process is based on an "opportunistic" combination of heuristics and strategies, carried out in small units during the execution of plans. In order to investigate the functional role of the prefrontal cortex in heuristic switching, 42 healthy controls performed a labyrinth crossing task (the Maps Test). During this computerized version of the Travelling Salesperson Problem, subjects had to decide which order of locations optimizes total travel time and distance. This task was performed with and without 1 Hz repetitive transcranial magnetic stimulation (rTMS), which exerts an inhibitory action on the targeted area, applied during the task over bilateral frontal sites (active stimulation) and parieto-occipital site (sham stimulation). Only repetitive bilateral rTMS over F3 and F4 significantly decreased the number of strategies with changes of heuristics, and increased the number of movements required to solve the task. This behaviour contrasts with the performance of healthy subjects in the planning task, but is consistent with the performance of frontal traumatic brain injury patients. The results indicate that, in a visuo-spatial problem-solving task, the prefrontal cortex is involved in the switching between heuristics during the execution of a plan.

D. Basso (✉) · M. Olivetti Belardinelli
ECONA, Interuniversity Center for Research
on Cognitive Processing in Natural and Artificial Systems,
Via dei Marsi, 78, Stanza 16,
2 Piano, 00185 Rome, Italy
E-mail: demis.basso@uniroma1.it
Tel.: +39-06-49917609
Fax: +39-06-4462449

M. Lotze · N. Birbaumer
Institut für Medizinische Psychologie
und Verhaltensneurobiologie, Tübingen, Germany

L. Vitale · M. Olivetti Belardinelli
Department of Psychology,
University of Rome "La Sapienza", Rome, Italy

F. Ferreri · P. M. Rossini
Neurology, University Campus Bio-Medico,
Rome, Italy

P. Bisiacchi
Department of General Psychology,
University of Padua, Padua, Italy

P. M. Rossini
IRCCS Centro S. Giovanni di Dio-Fatebenefratelli,
Brescia, Italy

Introduction

Planning has been defined as a "mental simulation, envisaging the circumstances and running through possible actions, evaluating the consequences and selecting the optimal order for executing them" (Cohen 1989, pp. 13–14). It has been demonstrated that the execution is simply a process involving pure mechanics of the movement, but rather, it is an active process that demands constant central monitoring (Cisek 2005). Recent studies (Basso et al. 2001; Phillips et al. 2001) proved that planning is largely carried out during path execution, rather than in a distinct stage in which entire plans of performance are made previously. Therefore, Hirtle and Gärling (1992) argued that human planning should be based on cognitive heuristics. A heuristic could be defined as a general principle regarded as being roughly correct although not completely accurate. In cognitive psychology, heuristics are described as behavioural schemas that approximate the correct solution, while they are more flexible and use fewer cognitive resources than algorithms. While planning processes are based on heuristics, a strategy is defined as an "opportunistic" combination of heuristics (Hayes-Roth and Hayes-Roth 1979). Therefore, a strategy is the specific way in which one or more heuristics have been used to produce the path. Subjects do not simply apply heuristics based on pattern recognition, they use continuous monitoring and change their behaviour in accordance with unexpected events, new information, or elements that were not previously considered (due to limits in working memory) in a general plan constructed before the execution phase.

One paradigm used to assess planning involves the Travelling Salesperson's Problem (TSP: Cadwallader 1975; MacGregor et al. 2004), in which the subject decides which order among a certain number of locations, optimizes the total travelling distance. In this planning task, subjects are required to achieve several different locations between the start and the final target, finding the shortest path in the shortest time. A computerized variant of the TSP, the Maps Test (Basso et al. 2001; Bisiacchi et al. 2002) is considered to be a laboratory analogue of the ability to organize spatial behaviour. In this version, in contrast with the classical TSP, the start and end points do not coincide, and subjects' movements are constrained to the horizontal and vertical directions. Therefore, the cognitive demand in the Maps Task is different and subjects' strategies will not correspond to those used in the classical TSP task.

This task was shown to be useful in the neuropsychological assessment of executive functions. Patients with closed frontal traumatic brain injuries (TBI) when faced with the Maps Paradigm were still able to achieve a solution but they showed a lower number of heuristic switching during their performance, with respect to the controls. According to the Supervisory Attentional System model of action control (SAS: Shallice 1988), the BA9 portion of the prefrontal cortex (PFC) is the cerebral region responsible for inhibiting existing plans.

Neuroimaging studies confirmed the involvement of the PFC in the activity taking place before and during the execution of an action, in relation to the organization of the schema to be performed (Koechlin et al. 2003). Prefrontal activation reflects, and is dependent upon, the goals and strategies adopted by the subject (Miller and Cohen 2001).

Our planning task is based on a survey approach, since subjects have to execute a plan in order to determine the best path among several different options to organize subgoals. We hypothesized that, while performing a TSP-like test, visuo-spatial planning for strategy change is predominantly performed in the dorsolateral portion of the PFC (DLPFC). In order to test the functional role of the cortical area below the midfrontal scalp region during the performance of a labyrinth-crossing task, a low-frequency repetitive transcranial magnetic stimulation (rTMS) was employed, which exerts an inhibitory action on the targeted area (Chen et al. 1997; Fitzgerald et al. 2002). Cortical inhibition induced by low-frequency stimulation was used in cognitive tasks like pain perception and modulation of slow cortical potentials (Karim et al. 2003; Rossi et al. 2000; Leocani et al. 2000). Boroojerdi et al. (2001) applied high-frequency rTMS to the DLPFC, obtaining an enhancement of the analogic reasoning performance, thus showing that rTMS can also interfere with high-level cognitive tasks. If the DLPFC is temporarily inhibited by a 1 Hz rTMS stimulation, the switch from the ongoing heuristic to a more efficient heuristic would be blocked only if the area is involved in the inhibition of a previously selected schema. Therefore, if stimulation is performed above the DLPFC during the labyrinthic task, 1 Hz rTMS stimulation should lead to a significant decrease in the number of switches between heuristics. We expected to find an effect of rTMS on heuristic switching, when applied over the bilateral dorsolateral PFC, but not over the control area corresponding to left superior occipital gyrus. Previous work indicates that the latter area is related to motion perception (McKeefry et al. 1997) and to semantic processing (Vandenberghe et al. 1996). Therefore, stimulation of this area should not interfere with the planning task.

Materials and methods

Participants

Ten healthy subjects (mean age (24.4, SD = 3.2), matched for sex, participated in the pilot study, while other 32 (years = 24.5 ± 4.7) participated in the experiment. All subjects were checked for TMS exclusion criteria (Wasserman 1998) and gave informed, written consent. The Ethics Committee of the Medical Faculty of the University of Tübingen approved the procedure.

Apparatus

The Maps Task used in this experiment is composed of 20 visuo-spatial problem-solving tasks (see Fig. 1 for an example). Each situation was composed of seven subgoals (positioned in different locations) plus a final goal. Starting at the top-left corner, subjects were instructed to move the silhouette (by pressing the arrow-keys) over each subgoal, and then to reach the final goal, located at the bottom-right corner. Subjects were also instructed to find and use the shortest route in the shortest time.

A Dantec MagPro stimulator (Skovlunde, Denmark) was used to generate repetitive biphasic magnetic pulses with a circular 10 cm magnetic coil. This coil was chosen in order to stimulate the right and left DLPFCs simultaneously, because it was impossible to place two focal coils without inducing mutual interference. At the beginning of the TMS session, the individual's resting motor threshold (MT) was determined for the thumb flexor muscle, according to international guidelines, as the stimulator's output capable of eliciting reproducible Motor Evoked Potentials (at least 50 μV in amplitude) in about 50% of ten consecutive stimuli (Rossini et al 1994). The stimulation intensity at 100% of MT mean = 43.8 ± 3.4) was used during the experiment with a frequency of 1 Hz.

Experimental procedure

Subjects were tested in two sessions, on two different days. In session A, 20 tasks of the Maps Test were administered without TMS-stimulation. In session B, the 20 tasks of the Maps Test were administered with TMS-stimulation. In

Fig. 1 Experimental setting. Subjects observed a two-dimensional labyrinth and had to move a human silhouette through all the subgoals to find the shortest route, starting from the upper left corner (*blue square*) to the bottom right corner (*red square*). During the task, 1 Hz rTMS was delivered over *Fz*, *PO3* or no stimulation was delivered. The *bottom line* depicts the time course of the experiment: *a* start of TMS stimulation; *b* appearance of the stimuli (start of the task); *c* end of the task; *d* repetitive TMS stimulation impulses

ten trials rTMS was delivered over the frontal scalp, the coil being positioned tangentially to the skull with its centre over the mid-frontal Fz position of the 10–20 International EEG system (in order to achieve a maximum stimulation over the two DLPFC, corresponding to both F3 and F4), with the A-side up, oriented parallel to the midline. The other 10 Maps Task were part of a control stimulation. In the pilot study the coil was tilted 45° away from the scalp, while in the experiment it was positioned over the left parieto-occipital scalp position (PO3 of the 10–20 International EEG system). Stimulation always began 3 s before each trial and ended when the subject reached the final goal (Fig. 1).

In the pilot study, the electrooculogram and scalp muscular reflexes were monitored by means of periocular skin Ag/Agcl electrodes in order to measure of the muscular twitches evoked by the TMS pulses (i.e. the blink reflex to stimulation of the ophthalmic trigeminal branch).

The order of session A (No-TMS) and session B (TMS) was randomized across the two days, while the order between the control-TMS and Fz-TMS conditions was randomized within the same session.

Data analysis

The statistical analysis considered the number of missed subgoals, the number of movements made, and the sequence of achieved subgoals. The Steppao variable (number of movements made minus the minimum number of movements required to solve the situation: Graham et al. 2000) was created in order to evaluate performance quality.

A series of four algorithms, (each one detecting the presence of a heuristic) was run on the paths independently producing one of the following three values: a heuristic applied to the whole path, one applied only to a part of it (but not to the whole path), or no heuristic applied. The four heuristics considered are the Nearest-Neighbour Heuristic, the Cluster Heuristic, and the Direction Heuristic, in its double form, horizontal and vertical (for details on heuristics and algorithms, see Basso 2005). Subsequently, the heuristics were compared in order to determine which one of the three strategies was used in each path: (1) unique strategy (one heuristic used from the beginning to the end of the path), (2) strategy with at least one switch between heuristics (a strategy in which heuristics are used for a part of the whole path, but, when jointly considered, they could cover the whole path), and (3) no strategy (heuristics used for a part of the path, but that could not cover all the path even when jointly considered, or no use of heuristics). A χ^2 was performed on the frequency of paths belonging to these categories, in order to find differences between the three stimulation conditions.

Results

Subjects were administered a mean of 11.6 (SD = 3.1) TMS pulses in each situation. In the pilot study, stimulus-related eye blinking, and scalp muscular reflexes evoked by the TMS pulse were not recorded by the EMG registration system in any of the situations. The lack of ocular responses also attests to the absence of other forms of facial distress, potentially caused by the activation of facial nerves more distant from the coil than the trigeminal nerve (directly under the coil). Hence, no statistical analysis can be performed on constant data, equal to zero, and the paths were analyzed in conjunction with the experimental sample.

Repetitive TMS over the frontal lobes resulted in a significant reduction of heuristic switching, compared to the other two conditions ($\chi^2 = 52.400$, $df = 2$, $P < 0.001$; Fig. 2). The paths to which no strategy was assigned were less than 7% in all conditions (No-TMS: 3.0%; TMS-PO3: 6.4%; TMS-Fz: 6.4%). In comparison to control conditions, PFC-stimulation resulted in a significant decrease in the Steppao variable [$F(2,1679) = 4.835$, $P > 0.05$]: when stimulated on the PFC, subjects were required to perform more movements to achieve the solution.

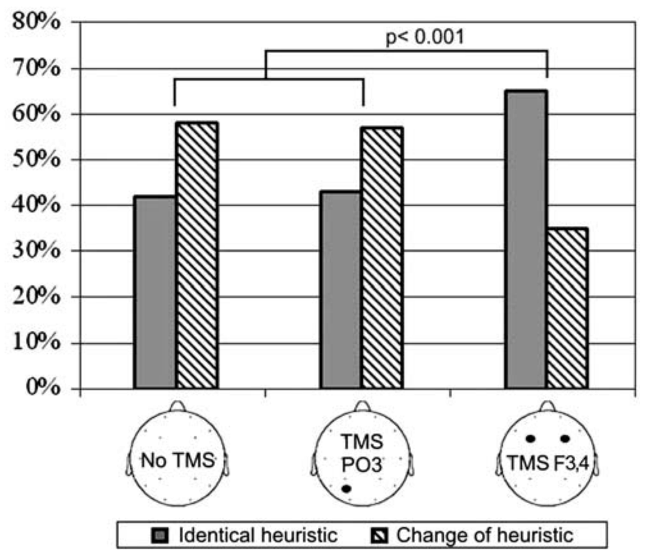

Fig. 2 Percentages of strategies used in the three experimental conditions. The *graph* indicates the percentage of each type of strategy used by subjects on the total number of paths presented, separate for each experimental condition of stimulation. The *percentages* represent the strategies used by the subjects based on an identical heuristic (*gray bars*) and based on changes between heuristics (*dashed bars*), with respect to the total number of paths performed by the subjects

Discussion

While performing a visuo-spatial planning task, bilateral rTMS stimulation over the frontal lobes (namely PFC areas) resulted in a less frequent use of strategies involving changes between heuristics. Given that during the execution subjects were limited in the selection of a more efficient heuristic, they were induced to produce longer paths. These effects can presumably be ascribed to the main involvement of the DLPFC, or to other brain areas connected with it. However, similar results have been achieved with different paradigms and techniques, i.e.: the Wisconsin Card Sorting Task, employed to assess the switching process (Dehaene and Changeux 1992), the Tower of London Planning Task (Morris et al. 1993), with traumatically injured frontal lobe patients (Shallice and Burgess 1991). Thus, these data provide a convergent series of support for the hypothesized inhibitory role of the prefrontal cortex as postulated by Shallice's model. In a TSP situation, heuristics are activated from the perceived configuration of stimuli and thus compete for execution on the basis of their activation level. The heuristic with the higher activation level is performed, and its execution is continuously monitored. As long as subgoals are achieved, the configuration of the remaining subgoals can change the heuristics' activation levels. Thus, PFC inhibits the previously selected heuristic and promotes a new heuristic.

Our results suggest that the DLPFC is involved in this switching process. However, Boroojerdi et al. (2001) obtained an effect by selectively stimulating the left DLPFC. In a further step, the Maps Task can be used to disentangle whether the on-line modification of plans primarily involves the left or the right PFC.

Acknowledgements The authors would like to thank Ralf Veit, Rita Fini, Angela Tagini, and three anonymous reviewers which have improved our work considerably. This work was partially supported by a Socrates–Erasmus Grant promoted by M.O.B.; D.B and P.S.B. are supported by the Italian PRIN2003; M.L. and N.B. are supported by the Deutsche Forschungsgemeinschaft (DFG).

References

Basso D (2005) Involvement of the prefrontal cortex in visuo-spatial planning. PhD Thesis, Department of Psychology, University of Rome "La Sapienza". Available at URL: http://www.padis.uniroma1.it/getfile.py?recid = 334
Basso D, Bisiacchi PS, Cotelli M, Farinello C (2001) Planning times during travelling salesman's problem: differences between closed head injury and normal subjects. Brain Cogn 46:38–42
Bisiacchi PS, Basso D, Cimolino S, Talamazzi M (2002) Gender differences in an environmental simulation. IAPS Bull People Environ Studies 21:1–3
Boroojerdi B, Phipps M, Kopylev L, Wharton CM, Cohen LG, Grafman J (2001) Enhancing analogic reasoning with rTMS over the left prefrontal cortex. Neurology 56:526–528
Cadwallader M (1975) A behavioral model of consumer spatial decision making. Econ Geogr 51:339–349
Chen R, Gerloff C, Classen J, Wassermann EM, Hallett M, Cohen LG (1997) Safety of different inter-train intervals for repetitive transcranial magnetic stimulation and recommendations for safe ranges of stimulation parameters. Electroencephalogr Clin Neurophysiol 105:415–421
Cisek P (2005) Neural representations of motor plans, desired trajectories, and controlled objects. Cogn Process 6:15–24
Cohen G (1989) Memory in the real world. Erlbaum, Hillsdale
Dehaene S, Changeux JP (1992) The Wisconsin card sorting test: theoretical analysis and modeling in a neuronal network. Cereb Cortex 1:62–79
Fitzgerald PB, Brown TL, Daskalakis ZJ, Chen R, Kulkarni J (2002) Intensity-dependent effects of 1 Hz rTMS on human corticospinal excitability. Clin Neurophysiol 113:1136–1141
Graham SM, Joshi A, Pizlo Z (2000) The traveling salesman problem: A hierarchical model. Mem Cogn 28:1191–1204
Hayes-Roth B, Hayes-Roth F (1979) A cognitive model of planning. Cogn Sci 3:275–310
Hirtle S, Gärling T (1992) Heuristic rules for sequential spatial decisions. Geoforum 23:227–238
Karim AA, Kammer T, Lotze M, Hinterberger T, Godde B, Cohen L, Birbaumer N (2003). Effects of repetitive transcranial magnetic stimulation (rTMS) on slow cortical potentials (SCP). Suppl Clin Neurophysiol 56:331–337
Koechlin E, Ody C, Kouneiher F (2003) The architecture of cognitive control in the human prefrontal cortex. Science 302(5648):1181–1185
Leocani L, Cohen LG, Wassermann EM, Ikoma K, Hallett M (2000) Human corticospinal excitability evaluated with transcranial magnetic stimulation during different reaction time paradigms. Brain 123:1161–1173
MacGregor JN, Chronicle EP, Ormerod TC (2004). Convex-hull or crossing-avoidance? Solution heuristics in the traveling salesperson problem. Mem Cogn 32:260–270
McKeefry DJ, Watson JD, Frackowiak RS, Fong K, Zeki S (1997) The activity in human areas V1/V2, V3, and V5 during the perception of coherent and incoherent motion. Neuroimage 5(1):1–12
Miller EK, Cohen JD (2001) An integrative theory of prefrontal cortex function. Annu Rev Neurosci 24:167–202
Morris RG, Ahmed S, Syed GM, Toone BK (1993) Neural correlates of planning ability: frontal lobe activation during the Tower of London test. Neuropsychologia 31(12):1367–1378

Phillips LH, Wynn VE, McPherson S, Gilhooly KJ (2001) Mental planning and the Tower of London task. Q J Exp Psychol A 54:579–598
Rossi S, Pasqualetti P, Rossini PM, Feige B, Ulivelli M, Glocker FX, Battistini N, Lucking CH, Kristeva-Feige R (2000) Effects of repetitive transcranial magnetic stimulation on movement-related cortical activity in humans. Cereb Cortex 10(8):802–808
Rossini PM, Barker AT, Berardelli A, Caramia MD, Caruso G, Cracco RQ, Dimitrijevic MR, Hallett M, Katayama Y, Lucking CH, Maertens De Noodhout AL, Marsden CD, Murray NMF, Rothwell JC, Swash M, Tomberg C (1994) Non-invasive electrical and magnetic stimulation of the brain, spinal cord and roots: basic principles and procedures for routine clinical application. Report of an IFCN committee. Electroencephalogr Clin Neurophysiol 91:79–92
Shallice T (1988) From neuropsychology to mental structure. Cambridge University Press, Cambridge
Shallice T, Burgess P (1991) Deficits in strategy application following frontal lobe damage in man. Brain 114:727–741
Vandenberghe R, Price C, Wise R, Josephs O, Frackowiak RS (1996) Functional anatomy of a common semantic system for words and pictures. Nature 383(6597):254–256
Wasserman EM (1998) Risk and safety in repetitive transcranial magnetic stimulation. Electroenceph Clin Neurophysiol 108:1–16