Neuropsychologia 49 (2011) 3525–3531

Contents lists available at SciVerse ScienceDirect

Neuropsychologia

journal homepage: www.elsevier.com/locate/neuropsychologia

The role of Area 10 (BA10) in human multitasking and in social cognition: A lesion study

María Roca[a,b,c,*], Teresa Torralva[a,b], Ezequiel Gleichgerrcht[a,b], Alexandra Woolgar[d], Russell Thompson[d], John Duncan[d], Facundo Manes[a,b,*]

[a] Institute of Cognitive Neurology (INECO), Buenos Aires, Argentina
[b] Institute of Neurosciences, Favaloro University, Buenos Aires, Argentina
[c] Laboratory of Neuroscience, Universidad Diego Portales, Santiago, Chile
[d] MRC Cognition and Brain Sciences Unit, 15 Chaucer Road, Cambridge CB2 7EF, UK

ARTICLE INFO

Article history:
Received 27 January 2011
Received in revised form 31 August 2011
Accepted 4 September 2011
Available online 10 September 2011

Keywords:
Frontal lobe
Theory of mind
Multitasking
Brodmann Area 10

ABSTRACT

A role for rostral prefrontal cortex (BA10) has been proposed in multitasking, in particular, the selection and maintenance of higher order internal goals while other sub-goals are being performed. BA10 has also been implicated in the ability to infer someone else's feelings and thoughts, often referred to as theory of mind. While most of the data to support these views come from functional neuroimaging studies, lesion studies are scant. In the present study, we compared the performance of a group of frontal patients whose lesions involved BA10, a group of frontal patients whose lesions did not affect this area (nonBA10), and a group of healthy controls on tests requiring multitasking and complex theory of mind judgments. Only the group with lesions involving BA10 showed deficits on multitasking and theory of mind tasks when compared with control subjects. NonBA10 patients performed more poorly than controls on an executive function screening tool, particularly on measures of response inhibition and abstract reasoning, suggesting that theory of mind and multitasking deficits following lesions to BA10 cannot be explained by a general worsening of executive function. In addition, we searched for correlations between performance and volume of damage within different subregions of BA10. Significant correlations were found between multitasking performance and volume of damage in right lateral BA10, and between theory of mind and total BA10 lesion volume. These findings stress the potential pivotal role of BA10 in higher order cognitive functions.

1. Introduction

The prefrontal cortex (PFC) is the cortical region in the frontal lobe anterior to the primary and association motor cortices. This brain area increases in size with phylogenetic development and, at least in humans, it is thought to be involved in planning complex cognitive behavior and in the expression of personality and appropriate social conduct. The prefrontal cortex is an anatomically and functionally heterogeneous structure and comprises cytoarchitectonically distinct regions, accounting for about 30% of our total cortical area (Fuster, 1997). Understanding the functional organization of the prefrontal cortex and the specific roles played by each of its distinct subregions (e.g. dorsolateral or rostral areas) is an essential issue in human cognitive neuroscience. Large volumes of data derived from functional neuroimaging have led to the statement of multiple influential theories regarding these issues. In order to draw stronger inferences, human lesion studies, which highlight the critical regions within brain networks, are crucial to complement functional neuroimaging approaches.

Brodmann Area 10 (BA10), also known as the frontal pole or rostral/anterior prefrontal cortex, is the largest and most anterior region within the human PFC (Semendeferi, Armstrong, Schleicher, Zilles, & Van Hoesen, 2001). Having experienced remarkable evolutionary expansion, this brain region also shows higher spine density than other areas of the human cortex and is highly interconnected with supramodal areas within the PFC in which information is believed to be represented at its most abstract level (Ramnani & Owen, 2004). All of the above suggests that BA10 plays an important role in human cognition. Accordingly, several authors have placed this brain region at the top of a frontal processing hierarchy (Badre & D'Esposito, 2007; Koechlin, Ody, & Kouneiher, 2003).

One function attributed to the anterior PFC is multitasking, in particular, the selection and maintenance of higher order internal goals while other sub-goals are being performed (e.g. Badre

* Corresponding authors at: Pacheco de Melo 1860, Capital Federal, BA, 1126, Argentina. Tel.: +54 11 4807 4748; fax: +54 11 4807 4748.
E-mail addresses: mroca@ineco.org.ar (M. Roca), fmanes@ineco.org.ar (F. Manes).

0028-3932/$ – see front matter © 2011 Elsevier Ltd. All rights reserved.
doi:10.1016/j.neuropsychologia.2011.09.003

Table 1
Patient characteristics.

Patient		Age	Sex	Aetiology	Side	Estimated premorbid IQ	Years POST Onset	Total lesion volume in ml	BA10 lesion volume in ml
BA10 group									
1	IB	39	F	Tumor	Bilateral	120	1	62.25	17.79
2	MS	64	F	Tumor	Right	111	5	9.50	2.66
3	DP	41	M	Tumor	Bilateral	115	1	66.83	7.21
4	SV	41	F	Tumor	Bilateral	128	2	60.02	14.95
5	SS	54	F	Tumor	Right	97	11	71.63	11.76
6	PM	54	M	Tumor	Left	121	9	31.34	9.4
7	ET	57	F	Infarct	Right	126	12	57.93	9.37
NonBA10 group									
1	PP	67	F	Tumor	Left	103	11	18.15	–
2	LB	29	F	Tumor	Right	88	8 months	78.76	–
3	AD	71	F	Infarct	Left	120	13	26.21	–
4	MS	77	M	Infarct	Right	121	11	12.95	–
5	GB	51	M	Tumor	Right	100	17	47.24	–
6	FG	47	F	Tumor	Right	106	9	87.65	–
7	RB	61	M	Tumor	Right	106	8	3.29	–
8	RH	75	F	Tumor	Right	118	27	32.57	–

& D'Esposito, 2009; Burgess, Dumonheil, & Gilbert, 2007; Gilbert, Frith, & Burgess, 2005; Gilbert et al., 2006, 2007; Koechlin & Summerfield, 2007). Maintenance and flexible retrieval of higher order goals enable us to orient our behavior to internal plans, rather than merely responding to the external environment. Most of the supporting data come from functional neuroimaging studies, and while multitasking and planning deficits have been described in patients with extensive frontal cortex damage (e.g. Goldstein, Bernard, Fenwick, Burgess, & McNeil, 1993; Hebb & Penfield, 1940; Shallice & Burgess, 1991), there are only a few lesion studies that have systematically assessed the specific role of BA10 in this domain. In a pioneering study, Burgess, Veitch, de Lacy Costello, and Shallice (2000) showed that damage to the more medial and polar aspects of BA8, 9 and 10, in the left hemisphere, was associated with more internal task switching deficits than right dorsolateral prefrontal lesions. However, the specific role of BA10 was not assessed, and the deficits found could also be related to simple rule breaking behavior, which was indeed part of the overall score reported. Recently, Dreher, Koechlin, Tierney, and Grafman (2008) also showed that in a group of patients with frontal lesions, deficits in multitasking correlated with the extent of damage in BA10. However, patients with closed head injuries were included in their study, making it hard to distinguish the effects of focal lesions and more diffuse damage. Two more recent lesion studies (Umeda, Kurosaki, Terasawa, Kato, & Miyahara, 2011; Volle, Gonen-Yaacovi, de Lacy Costello, Gilbert, & Burgess, 2011) have related rostral prefrontal cortex to prospective memory (the capacity to carry out intended actions after a delayed period of time), perhaps a critical element of multitasking.

Besides the maintenance and retrieval of higher order goals, functional neuroimaging has also linked BA10 to the ability to infer someone else's feelings and thoughts, demanding a complex set of functions collectively referred to as theory of mind. In fact, several functional neuroimaging studies have shown rostral PFC activation when the ability to infer other people's thoughts and emotions was assessed (e.g. Gilbert et al., 2006, 2007; Sommer et al., 2007). Again, while some lesion studies have shown that frontal damage can impair performance on theory of mind tasks (Narvid et al., 2009; Rowe, Bullock, Polkey, & Morris, 2001; Shamay-Tsoory, Tibi-Elhanany, & Aharon-Peretz, 2006; Shamay-Tsoory & Aharon-Peretz, 2007; Stone, Baron-Cohen, & Knight, 1998; Stuss, Gallup, & Alexander, 2001), no studies have yet investigated the role of BA10 in particular.

Based on neuroimaging findings, functional specialization within BA10 has been proposed both in the lateral-medial and anterior–posterior axes (Gilbert et al., 2007). Medial BA10, especially its posterior part, is supposed to play a major role in mentalizing and theory of mind (Gilbert et al., 2006, 2007). On the other hand, lateral BA10 seems necessary in human multitasking when attending to the outside world is not enough, and an internal goal is needed to direct behavior; that is, when cognition must be directed by stimulus-independent thought (Burgess et al., 2007; Dumontheil, Gilbert, Frith, & Burgess, 2010; Gilbert et al., 2005; Koechlin & Summerfield, 2007).

In the present study, we examined the role of BA10 both in multitasking and in theory of mind by comparing a group of frontal patients whose lesions affected BA10, a group of frontal patients whose lesions did not affect that area and a group of normal controls. We hypothesized that, if BA10 indeed plays a role in these cognitive functions, patients with lesions affecting this area would have impaired performance on tasks of multitasking and theory of mind relative to controls and patients with nonBA10 lesions. Moreover, given the findings from neuroimaging studies suggesting functional specialization across different BA10 subregions, we examined correlations between behavioral deficits and volume of damage within specific BA10 regions.

2. Material and methods

2.1. Subjects

Fifteen patients with chronic focal frontal lesions were recruited from the Cambridge Cognitive Neuroscience Research Panel at the MRC Cognition and Brain Sciences Unit in Cambridge, UK ($n = 11$) and from the INECO Research Data Base in Buenos Aires, Argentina ($n = 4$). All patients had a single focal lesion, verified by MRI, confined to frontal structures. Lesion aetiology was mostly tumor resection or cerebrovascular disease (Table 1). Exclusion criteria were current/previous psychiatric diagnosis, color blindness, additional neurological disease and history of diffuse brain damage. All patients gave informed consent prior to inclusion. Patients were selected from a larger cohort described in greater detail elsewhere (Roca et al., 2010) and were divided into groups on the basis of whether ("BA10" group) or not ("nonBA10" group) their lesions involved BA10 (*see below*).

Twenty-five healthy control volunteers were recruited from the volunteer panel of the MRC Cognition and Brain Sciences Unit ($n = 7$) and through advertisement in Buenos Aires ($n = 18$) and were matched with patients for age and estimated premorbid IQ. Premorbid intelligence was estimated using the revised National Adult Reading Test (NART; Nelson & Willison, 1991) for British subjects and the WAT-BA (Burin, Jorge, Arizaga, & Paulsen, 2000; Del Ser, González-Montalvo, Martínez-Espinosa, Delgado-Villapalos, & Bermejo, 1997) for Argentineans. Since patients were predominantly recruited from the UK, but controls from Argentina, British and Argentinean control subjects were compared on all measures in the study. No significant differences were found.

2.2. Neuroradiological assessment

MRI scans were performed for all patients and interpreted by a neurologist with experience in structural neuroimaging, who was blind to the experimental results

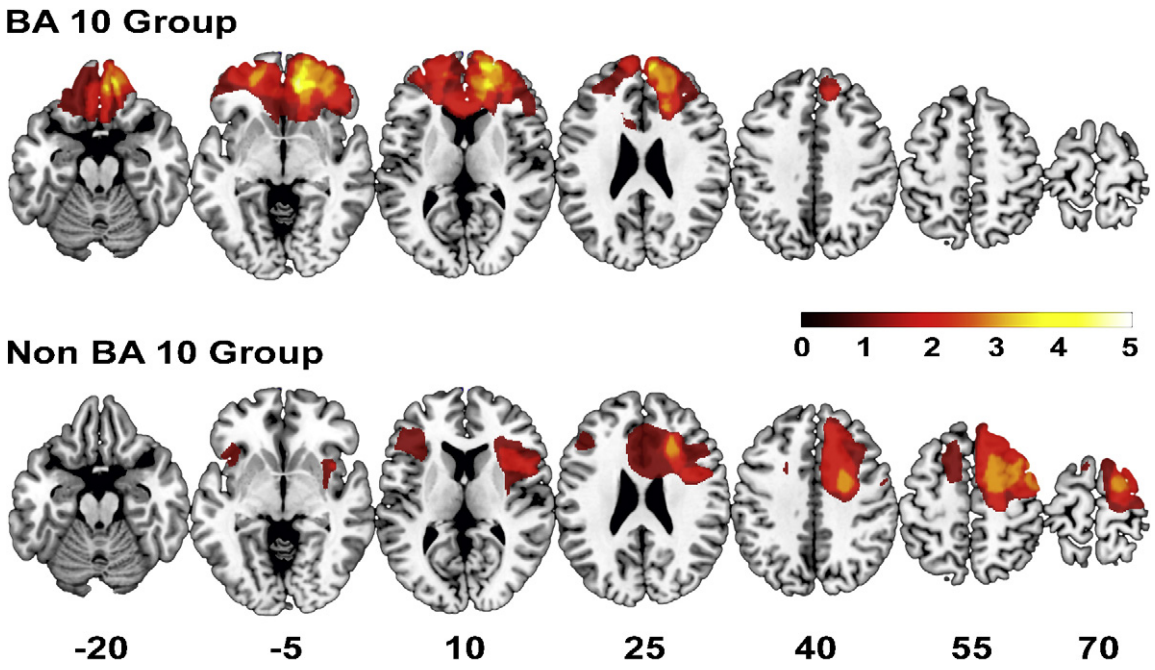

Fig. 1. Lesion overlaps for patients for patients with BA10 damage and with nonBA10 damage including white matter damage. Color scales show numbers of affected patients for each brain voxel. Numbers (bottom) represent *z* co-ordinates (mm) of each slice in MNI space.

(FM). Lesions were traced using MRIcro (Rorden & Brett, 2000) and normalized to a standard template using SPM5 software (Wellcome Department of Imaging Neuroscience, London, England; www.fil.ion.ucl.ac.uk) with cost-function masking to mask the lesion from the calculation of the normalization parameters (Brett, Leff, Rorden, & Ashburner, 2001). Using the Brodmann Area (BA) maps provided with MRIcroN (http://www.sph.sc.edu/comd/rorden/mricron), volume of damage in BA10 was calculated for each patient. Patients were then classified as having ($n = 7$) or not having ($n = 8$) BA10 damage (Table 1). Lesion overlaps for both groups are shown in Fig. 1.

For the purposes of a more detailed examination of BA10 lesions, separate lesion volumes were calculated for medial and lateral sub-divisions of BA10 in each hemisphere. To separate lateral from medial BA10, we used a fixed *X* coordinate of ±15 in Montreal Neurological Institute (MNI) atlas space ($-15 <= x <= 15$ for medial BA10, $x < -15$ or $x > 15$ for lateral BA10).

2.3. Neuropsychological assessment

2.3.1. The INECO Frontal Screening (Torralva, Roca, Gleichgerrcht, López, & Manes, 2009)

The INECO Frontal Screening (IFS) is a brief, sensitive, and specific tool designed to detect executive dysfunction which includes eight subtests. The design of the IFS represents three groups of tasks, as follows: (a) *response inhibition* (IFSRI), which includes motor programming, sensitivity to interference, motor inhibitory control and verbal inhibitory control subtest (maximum 15); (b) *abstract reasoning* (IFSAR), obtained from the proverb interpretation task (maximum 3) and; (c) working memory (IFSWM), including backwards digit span, verbal working memory and spatial working memory (maximum 12). All three of these components as well as the IFS total score (maximum 30) were calculated. (For further description of these subtests, see Torralva, Roca, Gleichgerrcht, López, et al., 2009 and Roca et al., 2010). For the IFS, data were available for 11/15 patients.

2.3.2. Hotel Task (Manly, Hawkins, Evans, Woldt, & Robertson, 2002; Torralva, Roca, Gleichgerrcht, Bekinschtein, & Manes, 2009)

The Hotel Task was developed from an earlier test that was designed to detect deficits in strategy production and multitasking among frontal patients with otherwise good executive test scores (Shallice & Burgess, 1991). The task requires maintenance of a higher-level goal while allocating time to a number of component sub-tasks. The task comprised five primary activities related to running a hotel: compiling bills, sorting coins for a charity collection, looking up telephone numbers, sorting conference labels, and proofreading. Subjects were told to try at least some of all five activities during a 15-min period, so that, at the end of this period, they would be able to give an estimate of how long each would take to complete. Subjects were explicitly told that there was not enough time to complete any of the five tasks. They were instructed that, instead, the main goal was to ensure that every task was at least partly sampled. Scoring for this task included (a) the total number of tasks performed for each subject, and (b) time allocation, calculated as the summed total deviation in seconds from the 3 min per task optimal time allocation. Total deviation was given a negative sign so that higher scores meant better performance. Data were available for 15/15 patients

2.3.3. Faux Pas (Stone et al., 1998)

The Faux Pas was originally designed to detect subtle theory of mind deficits in adults with Asperger syndrome. The test comprised 20 trials. In each of them, subjects were read a short, one-paragraph story. To reduce working memory demands, a written version of the story was also placed in front of the subjects. In 10 stories there was a Faux Pas, involving one person unintentionally saying something hurtful or insulting to another. In the remaining 10 stories there was no Faux Pas. After each story, subjects were asked whether something inappropriate was said, and if so, why that was the case. If the answer was incorrect, additional memory questions were asked to check that basic facts of the story had been retained. If they were not, the story was presented again and all questions repeated. The score was 1 point for each Faux Pas correctly identified, or non-Faux Pas correctly rejected. Data were available for 15/15 patients.

2.4. Statistical analysis

Variables were compared across the groups using one-way ANOVA with Tukey's *post hoc* method when relevant. Correlations were carried out using Pearson's *r*.

3. Results

Mean estimated premorbid IQ was 107.8 ($SD = 11.4$) for patients without damage in BA10, 117.0 ($SD = 10.5$) for patients with damage in BA10, and 114.0 ($SD = 12.0$) for control subjects (see Table 2). Differences between groups in premorbid IQ were not significant ($F_{2,37} = 1.3$, $p = 0.28$). Mean total lesion volume was not significantly different ($t_{12} = 0.74$, $p = 0.48$) between BA10 (56.84 ± 26.94 ml) and nonBA10 (43.33 ± 40.33 ml) patients. Within BA10 patients, no significant differences were found between volumes of lateral and medial BA10 damage ($t_6 = 1.04$, $p = 0.34$). Fig. 2 provides scores for each individual within the group and the groups' means for the IFS total score, the Hotel Task and the Faux Pas (see also Table 2).

For the IFS total score, ANOVA showed a significant effect of group (nonBA10, BA10, control) ($F_{2,33} = 5.03$, $p = 0.01$), with the nonBA10 group showing a significantly worse performance than control subjects ($p = 0.01$), but with no significant difference between the BA10 group and control subjects ($p = 0.48$) nor between the BA10 and nonBA10 groups ($p = 0.51$). When the response inhibition, abstract reasoning and working memory

Table 2
Mean performance scores (standard deviation in brackets). *p* Values represent ANOVA group differences for each task.

	BA10 group	NonBA10 group	Control subjects	*p*
Premorbid intelligence	117.0 (10.5)	107.8 (11.4)	114.0 (12.0)	0.28
IFS	24.7 (3.7)	22.9 (3.7)	26.4 (2.0)	0.01
Response inhibition (max. 15)	12.5 (2.4)	11.7 (2.0)	13.8 (9.2)	<0.01
Working memory (max. 12)	10.0 (1.4)	9.6 (1.4)	9.9 (1.4)	0.85
Abstract reasoning (max. 3)	2.3 (0.9)	1.6 (1.1)	2.7 (0.4)	<0.01
Hotel Task				
Attempted tasks	3.6 (1.2)	4.1 (0.8)	4.7 (0.6)	<0.01
Deviation from the optimal time (s)	−585.6 (337.3)	−492.7 (278.1)	−319.3 (169.5)	0.02
Faux Pas	17.3 (2.8)	18.5 (1.2)	19.1 (1.4)	0.04

subcomponents were compared between the three groups, significant differences were found both in the response inhibition ($p < 0.01$) and in the abstract reasoning subcomponents ($p < 0.01$). No significant differences were found for working memory ($p = 0.85$). In this regard, the nonBA10 group was outperformed by control subjects both in the response inhibition ($p < 0.01$) and in the abstract reasoning subtests ($p < 0.01$), while no significant differences were found between the BA10 group and control subjects nor between the BA10 and nonBA10 group for any of the variables.

For the Hotel Task, ANOVA also showed a significant effect of group both in the number of tasks attempted ($F_{2,37} = 6.17$, $p < 0.01$) and the deviation from the optimal time spent on each task ($F_{2,37} = 4.57$, $p = 0.02$). On both measures, the BA10, but not the nonBA10 group, was significantly outperformed by control subjects (both, $p < 0.05$), while no significant difference was found between the lesion groups ($p > 0.36$ for both cases). Similar results were observed for performance on the Faux Pas ($F_{2,37} = 3.39$, $p = 0.04$). Again, only the BA10 group showed significant deficits when compared with control subjects ($p = 0.04$), while no significant differences were found between the lesion groups ($p = 0.34$). Hotel Task performance, as measured by time deviation ($F_{2,32} = 4.0$, $p = 0.03$) and the number of tasks attempted ($F_{2,32} = 6.58$, $p < 0.01$) differed significantly between the three groups when the IFS was introduced as a covariate. In both cases, BA10 patients were outperformed by nonBA10 patients (time deviation: $p < 0.05$; tasks attempted: $p = 0.14$) and controls (time deviation: $p < 0.01$; tasks attempted: $p = 0.02$). For the Faux Pas, however, no significant differences between the groups were found with IFS as a covariate ($F_{2,32}$) = 0.05, $p = 0.96$).

In order to further analyze the difference in performance between the two lesion groups, patients' raw scores were converted to *z*-scores based on the data from normal controls. The IFS *z*-score was then subtracted from the Hotel Task *z*-score to provide an index of relative deficit in the two tasks, and a one-tailed *t*-test was used to compare relative deficits in the two patient groups. The test showed a significant difference in relative deficit between BA10 and nonBA10 groups, reflecting relatively worse performance on the Hotel Task/relatively better performance on IFS for the BA10 group. This was true for both Hotel Task scores: number of tasks attempted ($t(9) = 2.1$, $p = 0.03$) and deviation from optimal time allocation ($t(9) = 2.44$, $p = 0.02$). However, a similar test examining relative deficits on IFS vs. Faux Pas showed no significant difference between groups ($t(9) = 0.82$, $p = 0.22$).

Within the patient group as a whole, no significant correlations were found between total lesion volume and performance on any of the cognitive tasks (IFS: $r = -0.22$, $p = 0.54$; Faux Pas: $r = -0.25$, $p = 0.39$; Hotel Task number attempted: $r = -0.16$, $p = 0.58$; Hotel Task deviation from the optimal time: $r = -0.12$, $p = 0.67$). Within the BA10 group no significant correlations were found between total BA10 lesion volume and performance on the IFS or any of its subcomponents, or between total BA10 lesion volume and the Hotel Task (IFS total score: $r = 0.06$, $p = 0.93$; IFSRI: $r = 0.05$,

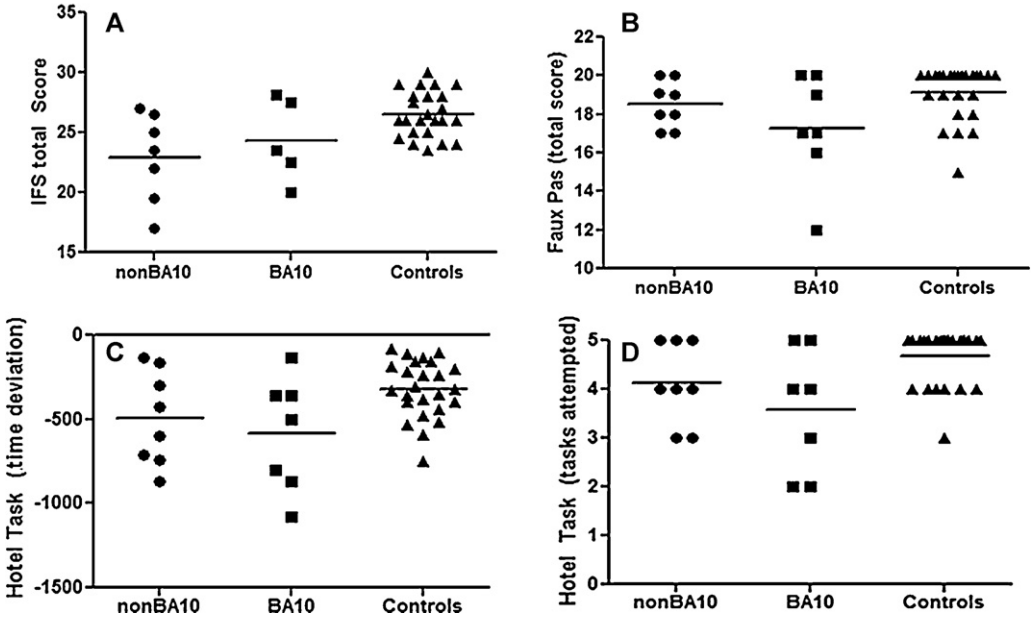

Fig. 2. Individual performance of participants in the nonBA10 (circles), BA10 (squares) and control (triangles) groups on the (A) INECO Frontal Screening, (B) Faux Pas, (C) Hotel Task (time deviation), and (D) Hotel Task (tasks attempted). Horizontal bars represent group means.

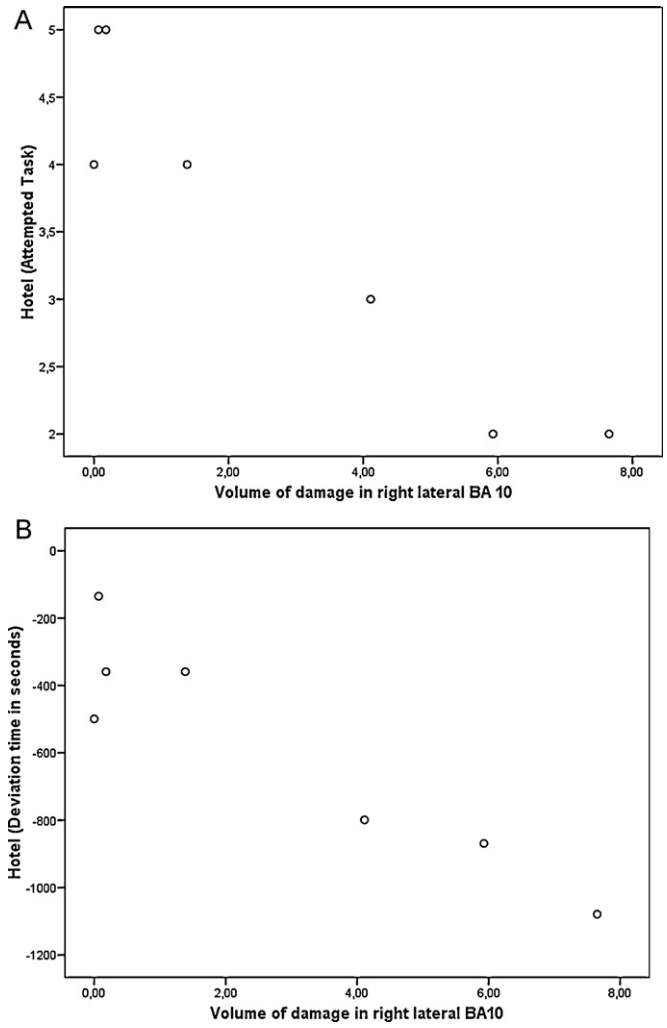

Fig. 3. Correlations between Hotel Task scores and volume of damage (in ml) in right lateral BA10: (A) number of tasks attempted; (B) deviation from optimal time allocation (in seconds).

$p = 0.88$; IFSAR: $r = 0.16$, $p = 0.63$; IFSWM: $r = 0.35$, $p = 0.28$; Hotel Task number attempted: $r = -0.17$, $p = 0.72$; Hotel Task deviation from the optimal time: $r = -0.10$, $p = 0.84$). Significant correlations were found between total BA10 lesion volume and performance on the Faux Pas ($r = -0.53$, $p = 0.04$). Lesion volume outside BA10 was correlated with worse abstract reasoning performance (IFSAR: $r = -0.66$, $p = 0.02$), but with none of the remaining cognitive measures (IFS total score: $r = -0.24$, $p = 0.46$; IFSRI: $r = -0.30$, $p = 0.36$; IFSWM: $r = 0.31$, $p = 0.35$; Faux Pas $r = -0.18$, $p = 0.51$; Hotel Task number attempted: $r = -0.14$, $p = 0.61$; Hotel Task deviation from the optimal time: $r = -0.13$, $p = 0.63$).

When lateral and medial regions were separated within the BA10 group, significant correlations were found between volume of damage in right lateral BA10 and both variables of the Hotel Task (tasks attempted: $r = -0.95$, $p < 0.01$; time allocation: $r = -0.94$, $p < 0.01$). Scatterplots are shown in Fig. 3A and B. No correlations were found for Hotel Task variables and volume of damage in medial BA10. Performance on the Faux Pas did not show significant correlations with lesion volume in any of the BA10 subregions.

4. Discussion

In the present study, we examined the role of BA10 in the ability to maintain higher order goals and in theory of mind. We also searched for correlations between task performance and volume of damage across different regions within BA10.

The present investigation shows that prefrontal lesions involving BA10 produce deficits both in theory of mind tasks and in multitasking, while frontal lesions not involving BA10 produced no such deficits. In particular, deficits in multitasking were specifically related to the extent of damage in right lateral BA10, while deficits in theory of mind were related to BA10 damage in general. On the other hand, nonBA10 patients showed worse performance than BA10 patients on an executive screening tool, particularly in its response inhibition and abstract reasoning subcomponents, which suggests that theory of mind and multitasking deficits following damage to BA10 cannot be explained simply by worse executive or general functioning.

The activation of BA10 during neuroimaging studies has prompted researchers to propose different models aimed at explaining the contribution of this brain region to cognition (Ramnani & Owen, 2004). BA10 has been associated with the ability to hold in mind goals while performing secondary objectives, allowing the subject to guide actions by internal or overarching plans, rather than merely responding to the external environment (Badre & D'Esposito, 2009; Burgess et al., 2007; Gilbert et al., 2005, 2006, 2007; Koechlin, Basso, Pietrini, Panzer, & Grafman, 1999; Koechlin, Corrado, Pietrini, & Grafman, 2000; Koechlin et al., 2003; Koechlin & Summerfield, 2007). Even more distinctively, it has been proposed that this brain region supports mechanisms that enable us to switch attention from external stimuli to self-generated internal representations, which has been known as the "gateway hypothesis" of BA10 (Burgess et al., 2007). This model proposes that lateral BA10 is particularly important when cognition must be directed by stimulus-independent thought and when an internal representation needs to be activated to achieve optimal behavior (Burgess et al., 2007; Dumontheil et al., 2010; Gilbert et al., 2005). In the Hotel Task, this function is captured by the requirement to make spontaneous switches between sub-tasks, guided by the higher-level goal of sampling each one.

Consistent with these accounts of rostral PFC activity, in our study, patients with damage to BA10 – but not patients whose lesions did not involve BA10 – made fewer task switches than control subjects in the Hotel Task, as evidenced by the decreased number of tasks sampled. Even more distinctively, our results showed that the extent of damage in right lateral BA10 significantly correlated with performance on the Hotel Task, supporting the suggestion that lateral BA10 might be particularly related with multitasking ability and goal/sub-goal management (Burgess et al., 2007; Dumontheil et al., 2010; Gilbert et al., 2005).

While rostromedial PFC has also been linked to the ability to infer someone else's feelings and thoughts, the exact role of BA10 in this ability has been less characterized. In this regard, rostromedial PFC is mainly understood as one part of a widely distributed neural network, including both right and left temporo-parietal junction as well as the precuneus, that supports the ability to infer another person's intentions (Ciaramidaro et al., 2007; Frith & Frith, 2003). In particular, medial BA10 has been associated with the ability to reflect on one's own mental states (Gusnard, Akbudak, Shulman, & Raichle, 2001; Johnson et al., 2002; Kelley et al., 2002), an ability which seems also to be necessary in order to make inferences about the mental states of others (Decety & Grezes, 1999; Frith & Frith, 2003; Mitchell, Banaji, & Macrae, 2005). In contrast, other authors have proposed that, while BA10 may be unnecessary to understand intentions related to private goals, it is responsible for the comprehension of social intentions (Ciaramidaro et al., 2007). A third view integrates theory of mind and multitasking models of BA10, proposing that the activation of BA10 during theory of mind tasks might be linked to the stimulus-independent cognitive

processing required to perform properly in such tests (Sommer et al., 2007).

While our results do not resolve these contradictory views, they do confirm the general importance of BA10 in social cognition. Patients with lesions involving BA10 showed deficits in their ability to detect when someone said something inappropriate and hurtful. This deficit was not shared by patients whose lesions did not involve BA10, though the lack of significant difference between the two patient groups cautions against too strong a conclusion of specificity. Unlike performance on the Hotel Task, no correlations were found between lesion volume in specific subregions of BA10 and performance on the Faux Pas. Thus, our data are not sufficient to support a particular association of medial BA10 with mentalizing or theory of mind.

Turning to the executive deficits that are measured by the IFS, it seems unlikely that BA10 lesions leave these entirely unaffected. In functional imaging, for example, left rostral PFC has been consistently associated with analogical reasoning, (Bunge, Wendelken, Badre, & Wagner, 2005; Green, Fugelsang, Kraemer, Shamosh, & Dunbar, 2006; Volle, Gilbert, Benoit, & Burgess, 2010; Wendelken, Nakhabenko, Donohue, Carter, & Bunge, 2008), an ability which is arguably necessary to resolve the proverb interpretation task. Our data allow no firm conclusions on this question: though nonsignificant, there was a clear trend for worse IFS scores in BA10 patients than in controls (Fig. 2), but its meaning is unclear since the lesions of these patients also extended outside BA10 (Table 1). It remains telling, nevertheless, that BA10 patients were outperformed by controls on multitasking and theory of mind tasks, but not on the IFS, while nonBA10 patients showed the reverse pattern. Our findings indicate that BA10 deficits cannot be entirely explained by a general worsening of executive functioning and that, at least for multitasking, they seem to be specific rather than general.

Several limitations of our results might be addressed in future studies. Though comparing favorably with other work in this area (e.g. Bird, Castelli, Malik, Frith, & Husain, 2004; Shallice & Burgess, 1991; Stone et al., 1998; Tranel, Hathaway Nepple, & Anderson, 2007), our study is still limited by a relatively small sample size. In this regard, it is possible that the lack of significant differences on the Faux Pas between the two patient groups might be addressed using larger sample sizes. Limited separation between damage to different areas within BA10 also makes it difficult to draw strong conclusions about functional specialization within this brain region. That said, strong associations between volume of damage of lateral BA10 and performance on the Hotel task is in striking agreement with recent neuroimaging reports relating lateral BA10 with multitasking abilities (Burgess et al., 2007; Dumontheil et al., 2010; Gilbert et al., 2005).

While functional neuroimaging data are merely correlational, studies of neurological patients are important to determine association. To the best of our knowledge, this is one of the few lesions studies to address the specific functions of BA10 and the first to show that lesions following damage to this brain area produce deficits in human multitasking and in theory of mind that cannot be explained by worsening of general performance. This is also the first lesion study to indicate a specific association of the lateral aspects of BA10 with the ability to maintain and retrieve higher internal goals, and to separate these cognitive functions from broader aspects of frontal executive control. In this regard, with the limitations outlined above, we believe that our study makes an important contribution to the understanding of a field otherwise dominated by functional neuroimaging.

Conflict of interest

The authors report no conflicts of interest.

Acknowledgments

This work was supported by the Medical Research Council (intramural program MC_US_A060_0001), and by an International Short Visit award from the Royal Society. FM was funded by a grant from Fundación INECO.

References

Badre, D. & D'Esposito, M. (2007). Functional magnetic resonance imaging evidence for a hierarchical organization of the prefrontal cortex. *Journal of Cognitive Neuroscience*, *19*, 2082–2099.

Badre, D. & D'Esposito, M. (2009). Is the rostro-caudal axis of the frontal lobe hierarchical? *Nature Reviews Neuroscience*, *10*, 659–669.

Bird, C. M., Castelli, F., Malik, O., Frith, U. & Husain, M. (2004). The impact of extensive medial frontal lobe damage on 'theory of mind' and cognition. *Brain*, *127*, 914–928.

Brett, M., Leff, A. P., Rorden, C. & Ashburner, J. (2001). Spatial norrmalization of brain images with focal lesions using cost function masking. *Neuroimage*, *14*, 486–500.

Bunge, S. A., Wendelken, C., Badre, D. & Wagner, A. D. (2005). Analogical reasoning and prefrontal cortex: Evidence for separable retrieval and integration mechanisms. *Cerebral Cortex*, *15*(3), 239–249.

Burgess, P. W., Dumonheil, I. & Gilbert, S. (2007). The gateway hypothesis of rostral prefrontal cortex (area 10) function. *Trends in Cognitive Sciences*, *11*, 290–298.

Burgess, P. W., Veitch, E., de Lacy Costello, A. & Shallice, T. (2000). The cognitive and neuroanatomical correlates of multitasking. *Neuropsychologia*, *38*, 848–863.

Burin, D. I., Jorge, R. E., Arizaga, R. A. & Paulsen, J. S. (2000). Estimation of premorbid intelligence: The word accentuation test – Buenos Aires version. *Journal of Clinical and Experimental Neuropsychology*, *22*, 677–685.

Ciaramidaro, A., Adenzato, M., Enrici, I., Erk, S., Pia, L., Bara, B. G., et al. (2007). The intentional network: How the brain reads varieties of intentions. *Neuropsychologia*, *1*(45), 3105–3113.

Decety, D. & Grezes, J. (1999). Neural mechanisms subserving the perception of human actions. *Trends in Cognitive Sciences*, *3*, 172–178.

Del Ser, T., González-Montalvo, J. I., Martínez-Espinosa, S., Delgado-Villapalos, C. & Bermejo, F. (1997). Estimation of premorbid intelligence in Spanish people with the Word Accentuation Test and its application to the diagnosis of dementia. *Brain and Cognition*, *33*, 343–356.

Dreher, J. C., Koechlin, E., Tierney, M. & Grafman, J. (2008). Damage to the fronto-polar cortex is associated with impaired multitasking. *PLoS One*, *3*(9), e3227.

Dumontheil, I., Gilbert, S., Frith, C. D. & Burgess, P. (2010). Recruitment of lateral rostral prefrontal cortex in spontaneous and task-related thoughts. *The Quarterly Journal of Experimental Psychology*, *63*(9), 1740–1756.

Frith, U. & Frith, C. D. (2003). Development and neurophysiology of mentalizing. *Philosophical Transactions of the Royal Society of London, Series B*, *358*, 459–473.

Fuster, J. M. (1997). *The prefrontal cortex-anatomy physiology, and neuropsychology of the frontal lobe* (3rd edition). Philadelphia: Lippincott-Raven.

Gilbert, S. J., Frith, C. D. & Burgess, P. W. (2005). Involvement of rostral prefrontal cortex in selection between stimulus-oriented and stimulus-independent thought. *European Journal of Neuroscience*, *21*(5), 1423–1431.

Gilbert, S. J., Spengler, S., Simons, J. S., Steele, J. D., Lawrie, S. M., Frith, C. D., et al. (2006). Functional specialization within rostral prefrontal cortex (area 10): A meta-analysis. *Journal of Cognitive Neuroscience*, *18*, 932–948.

Gilbert, S. J., Williamson, I. D., Dumontheil, I., Simons, J. S., Frith, C. D. & Burgess, P. W. (2007). Distinct regions of medial rostral prefrontal cortex supporting social and nonsocial functions. *Social Cognitive and Affective Neuroscience*, *2*(3), 217–226.

Goldstein, L. H., Bernard, S., Fenwick, P., Burgess, P. W. & McNeil, J. E. (1993). Unilateral frontal lobotomy can produce strategy application disorder. *Journal of Neurology, Neurosurgery & Psychiatry*, *56*, 274–276.

Green, A. E., Fugelsang, J. A., Kraemer, D. J., Shamosh, N. A. & Dunbar, K. N. (2006). Frontopolar cortex mediates abstract integration in analogy. *Brain Research*, *1096*(1), 125–137.

Gusnard, D. A., Akbudak, E., Shulman, G. L. & Raichle, M. E. (2001). Medial prefrontal cortex and self-referential mental activity: Relation to a default mode of brain function. *Proceedings of the National Academy of Sciences of the United States of America*, *98*, 4259–4264.

Hebb, D. O. & Penfield, W. (1940). Human behavior after extensive removal from the frontal lobes. *Archives of Neurology and Psychiatry*, *44*, 421–438.

Johnson, S. C., Baxter, L. C., Wilder, L. S., Pipe, J. G., Heiserman, J. E. & Prigatano, G. P. (2002). Neural correlates of self-reflection. *Brain*, *125*, 1808–1814.

Kelley, W. M., Macrae, C. N., Wyland, C. L., Caglar, S., Inati, S. & Heatherton, T. F. (2002). Finding the self? An event-related fMRI study. *Journal of Cognitive Neuroscience*, *14*, 785–794.

Koechlin, E., Basso, G., Pietrini, P., Panzer, S. & Grafman, J. (1999). The role of the anterior prefrontal cortex in human cognition. *Nature*, *399*, 148–151.

Koechlin, E., Corrado, G., Pietrini, P. & Grafman, J. (2000). Dissociating the role of the medial and lateral anterior prefrontal cortex in human planning. *Proceedings of the National Academy of Sciences of the United States of America*, *97*, 7651–7656.

Koechlin, E., Ody, C. & Kouneiher, F. (2003). The architecture of cognitive control in the human prefrontal cortex. *Science*, *202*, 1181–1185.

Koechlin, E. & Summerfield, C. (2007). An informational theoretical approach to prefrontal executive function. *Trends in Cognitive Sciences*, *11*, 2209–2235.

Manly, T., Hawkins, K., Evans, J., Woldt, K. & Robertson, I. H. (2002). Rehabilitation of executive function: A facilitation of effective goal management on complex tasks using periodic auditory alerts. *Neuropsychologia*, *40*, 2671–2681.

Mitchell, J. P., Banaji, M. R. & Macrae, C. N. (2005). The link between social cognition and self-referential thought in the medial prefrontal cortex. *Journal of Cognitive Neuroscience*, *17*, 1306–1315.

Narvid, J., Gorno-Tempini, M. L., Slavotinek, A., Dearmond, S. J., Cha, Y. H., Miller, B. L., et al. (2009). Of brain and bone: The unusual case of Dr. A. *Neurocase*, *15*(3), 190–205.

Nelson, H. E. & Willison, J. R. (1991). *The Revised National Adult Reading Test–Test manual. NFER-Nelson*. UK: Windsor.

Ramnani, N. & Owen, A. M. (2004). Anterior prefrontal cortex: Insights into function from anatomy and neuroimaging. *Nature Reviews*, *5*, 184–194.

Roca, M., Parr, A., Thompson, R., Woolgar, A., Torralva, T., Antoun, N., et al. (2010). Executive function and fluid intelligence after frontal lobe lesions. *Brain*, *133*, 234–247.

Rorden, C. & Brett, M. (2000). Stereotaxic display of brain lesions. *Behavioral Neurology*, *12*, 191–200.

Rowe, A. D., Bullock, P. R., Polkey, C. E. & Morris, R. G. (2001). Theory of mind impairments and their relationship to executive functioning following frontal lobe excisions. *Brain*, *124*(Pt 3), 600–616.

Semendeferi, K., Armstrong, E., Schleicher, A., Zilles, K. & Van Hoesen, G. (2001). Prefrontal cortex in humans and apes: A comparative study of area 10. *American Journal of Physical Anthropology*, *114*, 224–241.

Shallice, T. & Burgess, P. W. (1991). Deficits in strategy application following frontal lobe damage in man. *Brain*, *114*, 727–741.

Shamay-Tsoory, S. G., Tibi-Elhanany, Y. & Aharon-Peretz, J. (2006). The ventromedial prefrontal cortex is involved in understanding affective but not cognitive theory of mind stories. *Social Neuroscience*, *1*(3–4), 149–166.

Shamay-Tsoory, S. G. & Aharon-Peretz, J. (2007). Dissociable prefrontal networks for cognitive and affective theory of mind: A lesion study. *Neuropsychologia*, *45*(13), 3054–3067.

Sommer, M., Döhnel, K., Sodian, B., Meinhardt, J., Thoermer, C. & Hajak, G. (2007). Neural correlates of true and false belief reasoning. *Neuroimage*, *35*(3), 1378–1384.

Stone, V. E., Baron-Cohen, S. & Knight, R. T. (1998). Frontal lobe contributions to theory of mind. *Journal of Cognitive Neuroscience*, *10*(5), 640–656.

Stuss, D. T., Gallup, G. G., Jr. & Alexander, M. P. (2001). The frontal lobes are necessary for 'theory of mind'. *Brain*, *124*(Pt 2), 279–286.

Torralva, T., Roca, M., Gleichgerrcht, E., Bekinschtein, T. & Manes, F. (2009). A neuropsychological battery to detect specific executive and social cognitive impairments in early frontotemporal dementia. *Brain*, *132*, 1299–1309.

Torralva, T., Roca, M., Gleichgerrcht, E., López, P. & Manes, F. (2009). INECO Frontal Screening (IFS): A brief, sensitive, and specific tool to assess executive functions in dementia. *Journal of the International Neuropsychological Society*, *28*, 1–10.

Tranel, D., Hathaway Nepple, J. & Anderson, S. W. (2007). Impaired behavior on real-world tasks following damage to the ventromedial prefrontal cortex. *Journal of Clinical and Experimental Neuropsychology*, *29*, 319–332.

Umeda, S., Kurosaki, Y., Terasawa, Y., Kato, M. & Miyahara, Y. (2011). Deficits in prospective memory following damage to the prefrontal cortex. *Neuropsychologia*, *49*(8), 2178–2184.

Volle, E., Gilbert, S. J., Benoit, R. G. & Burgess, P. W. (2010). Specialization of the rostral prefrontal cortex for distinct analogy processes. *Cerebral Cortex*, *20*(11), 2647–2659.

Volle, E., Gonen-Yaacovi, G., de Lacy Costello, A., Gilbert, S. J. & Burgess, P. W. (2011). The role of rostral prefrontal cortex in prospective memory: A voxel-based lesion study. *Neuropsychologia*, *49*(8), 2185–2198.

Wendelken, C., Nakhabenko, D., Donohue, S. E., Carter, C. S. & Bunge, S. A. (2008). Brain is to thought as stomach is to?: Investigating the role of rostrolateral prefrontal cortex in relational reasoning. *Journal of Cognitive Neuroscience*, *20*(4), 682–693.