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Dorsolateral prefrontal contributions to human intelligence

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ABSTRACT

Although cognitive neuroscience has made remarkable progress in understanding the involvement of the prefrontal cortex in executive control functions for human intelligence, the necessity of the dorsolateral prefrontal cortex (dlPFC) for key competencies of general intelligence and executive function remains to be well established. Here we studied human brain lesion patients with dlPFC lesions to investigate whether this region is computationally necessary for performance on neuropsychological tests of general intelligence and executive function, administering the Wechsler Adult Intelligence Scale (WAIS) and subtests of the Delis Kaplan Executive Function System (D-KEFS) to three groups: dlPFC lesions ($n=19$), non-dlPFC lesions ($n=152$), and no brain lesions ($n=55$). The results indicate that: (1) patients with focal dlPFC damage exhibit lower scores, at the latent variable level, than controls in general intelligence (g) and executive function; (2) dlPFC patients demonstrate lower scores than controls in several executive measures; and (3) these latter differences are no longer significant when the pervasive influence of the general factor of intelligence (g) is statistically removed. The observed findings support a central role for the dlPFC in global aspects of general intelligence and make specific recommendations for the interpretation and application of the WAIS and D-KEFS to the study of high-level cognition in health and disease.

1. Introduction

The search for organizing principles that govern human intelligence represents a central and enduring aim of cognitive neuroscience, with emerging research providing new insight into the neural architecture of goal-directed, intelligent behavior (see Barbey et al., 2012; Barbey & Grafman, in press a, in press b; Barbey, Krueger, & Grafman, 2009a, 2009b; Colom & Thompson, 2011; Colom, Karama, Jung, & Haier, 2010; Miller, 2000; Miller & Cohen, 2001, for reviews). Extensive functional neuroimaging evidence indicates that the dorsolateral prefrontal cortex (dlPFC) plays a central role in executive control functions for human intelligence (for meta-analytic reviews, see Owen, 1997; Owen, McMillan, Laird, & Bullmore, 2005; Wager & Smith, 2003; Wager, Jonides, & Reading, 2004). Fundamental questions, however, remain in the absence of definitive neuropsychological evidence to corroborate the importance of the dlPFC for higher cognition. A seminal and long-standing issue concerns whether the dlPFC is computationally necessary for key competencies of general intelligence and executive function, and, in particular, whether this region provides an integrative neural architecture for core features of human intelligence (for a recent review, see Deary, Penke, & Johnson, 2010).

Theories of intelligence and executive function have focused on the identification of a general factor, referred to as *psychometric g*, that has been shown to underlie performance on a broad range of cognitive tests (Spearman, 1904, 1927; for a review, see Jensen, 1998; Neisser et al., 1996; Nisbett et al., 2012). Neuroscience models deriving from Spearman's classic theory (1927) attribute diverse functional roles to the dlPFC, positing that this cortical region provides a unified neural architecture for higher cognition (e.g., Duncan et al., 2000; Duncan, 2010). Accumulating neuroscience data support this framework, demonstrating recruitment of the dlPFC for performance on tests of general intelligence (e.g., Prabhakaran, Smith, Desmond, Glover, & JDE, 1997; Esposito, Kirkby, Van Horn, Ellmore, & Berman, 1999; Duncan et al., 2000; Bishop, Fossella, Croucher, & Duncan, 2008) and executive function (e.g., Duncan & Owen, 2000; Duncan,

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2006). Monkey electrophysiological data further indicate that cells within the dlPFC adaptively code different kinds of task-relevant information in different behavioral contexts (e.g., Duncan, 2001; Miller & Cohen, 2001), supporting the involvement of this region in a wide range of higher cognitive functions.

The alternative to Spearman's (1927) single factor model proposes that tests of general intelligence reflect the average or combined activity of separate cognitive processes (Thomson, 1951, see also Bartholomew, Deary, & Lawn, 2009; van der Maas et al., 2006). According to this framework, general intelligence is supported by a variety of different cognitive functions that are mediated by a broadly distributed network of functionally specialized brain regions (e.g., Colom & Thompson, 2011; Colom et al., 2009; Gläscher et al., 2009, 2010; Jung & Haier, 2007). This model predicts that the dlPFC will be selectively involved in specific cognitive operations rather than providing an integrative architecture for general intelligence and executive function. An increasing number of neuropsychological studies support this framework, reporting patients with damage to prefrontal cortices who demonstrate selective deficits in general intelligence or executive function, suggesting that these domains of higher cognition recruit functionally distinct neural systems (e.g., Blair & Cipolotti, 2000; Burgess & Shallice, 1996; Eslinger & Damasio, 1985; Shallice & Burgess, 1991).

Of the neuropsychological patient studies that have examined prefrontal contributions to general intelligence (e.g., Basso, De Renzi, Faglioni, Scotti, & Spinnler, 1973; Bechara, Damasio, Damasio, & Anderson, 1994; Black, 1976; Blair & Cipolotti, 2000; Bugg, Zook, DeLosh, Davalos, & Davis, 2006; Burgess & Shallice, 1996; Duncan, Burgess, & Emslie, 1995; Duncan, Emslie, Williams, Johnson, & Freer, 1996; Eslinger & Damasio, 1985; Gläscher et al., 2010, 2009; Isingrini & Vazou,1997; Kane & Engle, 2002; Parkin & Java, 1999; Roca et al., 2009; Shallice & Burgess, 1991; Tranel, Manzel, & Anderson, 2008) and executive function (e.g., Baldo & Dronkers, 2006; D'Esposito & Postle,1999; D'Esposito, Cooney, Gazzaley, Gibbs, & Postle, 2006; Muller, Machado, & Knight, 2002; Ptito, Crane, Leonard, Amsel, & Caramanos, 1995; Tsuchida & Fellows, 2009; Volle et al., 2008), all share one or more of the following features: diffuse (rather than focal) dlPFC lesions, lack of comparison subjects carefully matched for pre- and post-injury performance measures, and exclusive use of general intelligence or executive function tests. As a consequence, there has been no comprehensive evaluation of general intelligence and executive function in a relatively large sample of patients with damage specifically involving the dlPFC, and across a broad range of tasks and stimulus material. Furthermore, intelligence and executive function share relevant variance, which may greatly confound their contribution to the observed findings (Colom et al., 2009; Haier et al., 2009). Therefore, it is critical to analyze specific variance of the constructs and measures of interest. The absence of such data represents a substantial gap in the understanding of both dlPFC function and the neural substrates of higher cognition.

The aim of the present investigation is to characterize key competencies of general intelligence and executive function in a sample of patients with focal dlPFC lesions, examining whether this region (i) provides an integrative architecture for general intelligence (*g*) or instead (ii) mediates a specific class of cognitive operations within a particular high-level domain (e.g., executive function, working memory, perceptual organization, processing speed).

2. Materials and methods

2.1. Participant data

We drew brain-injured participants from the Vietnam Head Injury Study (VHIS) registry, which includes American veterans who suffered brain damage from penetrating head injuries in the Vietnam War ($n=199$), as well as neurologically healthy Vietnam veterans ($n=54$). The VHIS has been organized in three phases. Phase 1 (1967–1970) was the initial enrollment; Phase 2 (1981–1984) included a cognitive evaluation; and Phase 3 (2003–2006) included a more comprehensive evaluation as well as CT brain imaging. Further details regarding the VHIS participants, including methods for visualizing and quantifying brain lesions, have previously been reported (Barbey et al., in press b, 2012, 2009). Subjects were eligible for the present study if they participated in Phases 2 and 3 evaluations.

To preclude the possibility that impaired performance on general intelligence and executive function tests could be secondary to deficits in the production and/or comprehension of language, we excluded any participant who had significant impairment on a test of language production and language comprehension (defined as performance at least two standard deviations below the mean of the neurologically healthy group on the Boston Naming Test). From the remaining brain-injured veterans we selected those with damage primarily localized to the dlPFC (BA 9/46) in the left and/or right hemisphere(s) (dlPFC Lesion group; Fig. 1; $n=19$). The dlPFC is located on the lateral and dorsal part of the medial convexity of the frontal lobe and comprises BA 9 and 46 and a few transitional areas: 9–8, 9–45, 46–10, and 46–45 (for a detailed description of anatomical boundaries, see Rajkowska & Goldman-Rakic, 1995a, b). In addition, we investigated a comparison group of brain-injured veterans whose damage was primarily within the PFC but involved ventral (rather than dorsal) regions (Non-dlPFC Lesion group; $n=152$; Supplemental Fig. 1). Neurologically healthy veterans served as an additional comparison group (Control group; $n=54$). Demographic and background cognitive function data for the three groups are presented in Supplemental Table 1. No significant between-group differences were observed with respect to basic demographic variables (age, sex, years of education), pre- and post-combat measures of cognitive function, and total percent volume loss. All patient groups were therefore well matched with respect to (1) demographic variables, (2) pre- and post-combat measures of cognitive function, and (3) lesion size. All participants understood the study procedures and gave their written informed consent, which was approved by the Institutional Review Board at the National Naval Medical Center and the National Institute of Neurological Disorders and Stroke.

2.2. Lesion analysis

We acquired computed tomography (CT) data during the Phase 3 testing period. Axial CT scans without contrast were acquired at the Bethesda Naval Hospital on a General Electric Medical Systems Light Speed Plus CT scanner in helical mode. We reconstructed the images with an in-plane voxel size of 0.4×0.4 mm, an overlapping slice thickness of 2.5 mm and a 1-mm slice interval. We determined lesion location and volume from CT images using the Analysis of Brain Lesion (ABLe) software (Makale et al., 2002; Solomon, Raymont, Braun, Butman, & Grafman, 2007) contained in MEDx v3.44 (Medical Numerics) with enhancements to support the Automated Anatomical Labeling (AAL) atlas (Tzourio-Mazoyer et al., 2002). We applied the AAL atlas of the human brain to obtain neuroanatomical labels for locations in 3-dimensional space. For the hypotheses about specific brain areas (dlPFC), we defined regions of interest in terms of AAL structures (Tzourio-Mazoyer et al., 2002) and Talairach coordinates (Talairach & Tournoux, 1988). As part of this process, we spatially normalized the CT image of each subject's brain to a CT template brain image in Montreal Neurological Institute space (Collins, Neelin, Peters, Evans, & Automatic, 1994). We determined the percentage of AAL structures that the lesion entailed by analyzing the overlap between the spatially normalized lesion image and the AAL atlas image. We calculated lesion volume by manually tracing the lesion in all relevant slices of the CT image and then summing the traced areas and multiplying by slice thickness. The tracing technique isolated areas of missing brain and regions affected by metallic artifacts and penetrating objects. A trained neuropsychiatrist carried out the manual tracing, which was then reviewed by an observer that was blind to the results of the neuropsychological testing. In addition, we further characterized the contribution of white matter pathways in the dlPFC patient sample, identifying that each patient group entailed damage within or adjacent to the (1) superior longitudinal fasciculus (branch 1 and 2), (2) frontal aslant tract, (3) fronto-striatal projections, (4) callosal connections, and (4) U-shaped connections between superior and middle frontal gyri (see Mori et al., 2008).

2.3. Neuropsychological tests

We administered the Wechsler Adult Intelligence Scale, 3rd Edition (WAIS; Wechsler, 1997) and subtests of the Delis Kaplan Executive Function System (D-KEFS; Delis, Kaplan, & Kramer, 2001) to investigate the necessity of dlPFC for key competencies of general intelligence and executive function. The reported neuropsychological data from the WAIS and D-KEFS represent standardized scores based on the published norms in Wechsler (1997) and Delis et al. (2001), respectively.

2.3.1. Wechsler Adult Intelligence Scale, 3rd edition

The WAIS embodies a four-tier hierarchy, providing a Full Scale Intelligence Index (Tier 1) derived from Verbal and Performance Intelligence Indices (Tier 2) that

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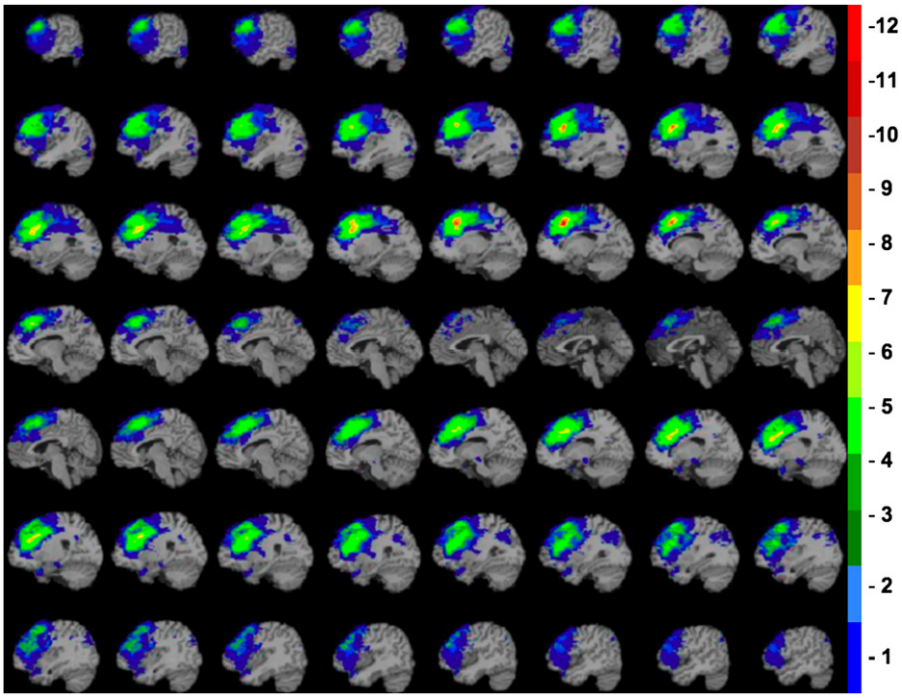

Fig. 1. Diagram of the lesion overlap map for the dorsolateral prefrontal patients. The color indicates the number of veterans in the dorsolateral prefrontal group ($n=19$) with damage to a given voxel. The depicted sagittal slices progress from the right lateral regions (top left) to the midline and left lateral areas (bottom right). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.).

Table 1
Descriptive statistics for measures of general intelligence and executive function.

Descriptives	Group	*N*	Mean	SD
Latent *g*	**dlPFC**	19	91.31	15.39
	non-dlPFC	152	99.31	14.96
	Control	55	104.91	13.42
Latent verbal comprehension	**dlPFC**	19	95.28	18.82
	Non-dlPFC	152	99.82	14.96
	Control	55	102.14	13.44
Latent perceptual organization	**dlPFC**	19	93.46	15.48
	Non-dlPFC	152	99.32	15.23
	Control	55	104.14	13.24
Latent working memory	**dlPFC**	19	91.52	17.64
	Non-dlPFC	152	99.22	14.51
	Control	55	105.09	13.85
Latent processing speed	**dlPFC**	19	91.92	13.94
	Non-dlPFC	152	98.56	15.04
	control	55	106.77	12.83
Latent executive function	**dlPFC**	19	91.31	15.39
	Non-dlPFC	152	99.31	14.96
	Control	55	104.91	13.42

each consist of component operations (Tier 3) measured by intelligence subtests (Tier 4). Verbal Intelligence examines general knowledge, vocabulary, and the ability to reason using words and numbers, and is assessed by Verbal Comprehension and Working Memory subtests. Performance Intelligence examines the ability to solve problems in novel situations, independent of acquired knowledge, and is assessed by Perceptual Organization and Processing Speed subtests. Additional Performance Intelligence subtests of the WAIS that are not part of the four factor indices include Picture Arrangement and Object Assembly. Supplemental Table 2 provides a brief description of these tests (for further detail concerning the descriptions of each test, their standardization, reliability, and validity, see Wechsler, 1997).

2.3.2. Delis Kaplan Executive Function System

The D-KEFS consists of executive function tests that examine a broad range of high-level cognitive skills. Our analysis focused on five executive function measures that, in recent studies, have been found to be particularly sensitive to frontal lobe damage (e.g., Baldo, Shimamura, Delis, Kramer, & Kaplan, 2001; Cato, Delis, Abildskov, & Bigler, 2004; Delis, Squire, Bihrle, & Massman, 1992; McDonald, Delis, Norman, Tecoma, & Iragui, 2005a; McDonald et al., 2005b, 2005c). These tests include the *Trail Making Test*, *Verbal Fluency Test*, *Sorting Test, Twenty Questions Test,* and *Tower Test.* Supplemental Table 3 provides a brief description of each test (for further detail concerning the description of each test, their standardization, reliability, and validity, see Delis et al., 2001, 2007; Homack, Lee, & Riccio, 2005; Swanson, 2005).

2.4. Statistical analysis

First, WAIS and D-KEFS measures were analyzed using a latent variable approach. A key advantage of this approach is that specific task requirements for the administered WAIS and D-KEFS subtests have less influence on the estimates of the construct relations (general intelligence and executive function). This approach also partials out measurement error for each specific measure, and therefore latent variables provide a reliable estimate of the constructs of interest. Here we computed SEM using the AMOS program (Arbuckle, 2006). Several fit indices were considered. First, the χ^2/DF index is frequently considered as a rule of thumb, because it corrects the high sensitivity of the chi-square statistic for large sample sizes (Jöreskog, 1993). Values showing a good fit must be around 2.0. Second, RMSEA is usually recommended because it is sensitive to misspecification of the model. Values between 0 and 0.05 indicate good fit; values between 0.05 and 0.08 represent acceptable errors; and values greater than 0.10 are indicative of poor fit (Byrne, 1998). Finally, comparative fit index (CFI) is also reported; acceptable values must be larger than 0.90 (Marsh et al., 1988). Verbal comprehension, perceptual organization, working memory, and processing speed measures from the WAIS were grouped in four first-order factors. Afterwards, a higher-order factor (representing the general factor of intelligence, *g*) predicted these four factors. Further, D-KEFS measures were collapsed in a latent executive factor. Finally, this latter factor was correlated with *g*.

Second, scores for the enumerated latent factors were obtained using the AMOS program (Arbuckle, 2006). The three groups of participants were systematically compared in general intelligence, verbal comprehension, perceptual organization, working memory, processing speed, and executive function.

Third, scores for verbal comprehension, perceptual organization, working memory, processing speed, and specific executive measures were computed while statistically removing the effect of the general factor of intelligence (*g*). This was accomplished by performing regression analyses. The three groups of participants are compared on these residual scores.

2.4.1. Analysis of variance

For the measures enumerated above, we conducted a one-way ANOVA examining the performance of dlPFC lesion patients ($n=19$) with respect to non-dlPFC lesion patients ($n=152$) and neurologically healthy participants

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Table 2
Inferential statistics for measures of general intelligence and executive function.

Bonferroni	(I) Group	(J) Group	Mean difference (I–J)	Standard error	Sig.	Confidence interval 95%	
						Upper limit	Lower limit
Latent *g*	**dlPFC**	**non-dlPFC**	−7.99	3.56	0.08	−16.59	0.60
		Control	−13.60	3.90	0.00	−23.00	−4.20
	Non-dlPFC	**dlPFC**	7.99	3.56	0.08	−0.60	16.59
		Control	−5.61	2.30	0.05	−11.16	−0.05
	Control	**dlPFC**	13.60	3.90	0.00	4.20	23.00
		non-dlPFC	5.61	2.30	0.05	0.05	11.16
Latent verbal comprehension	**dlPFC**	**non-dlPFC**	−4.53	3.64	0.64	−13.32	4.25
		Control	−6.85	3.98	0.26	−16.46	2.75
	Non-dlPFC	**dlPFC**	4.53	3.64	0.64	−4.25	13.32
		Control	−2.32	2.35	0.98	−8.00	3.36
	Control	**dlPFC**	6.85	3.98	0.26	−2.75	16.46
		non-dlPFC	2.32	2.35	0.98	−3.36	8.00
Latent perceptual organization	**dlPFC**	**non-dlPFC**	−5.86	3.60	0.31	−14.54	2.82
		Control	−10.68	3.94	0.02	−20.18	−1.19
	Non-dlPFC	**dlPFC**	5.86	3.60	0.31	−2.82	14.54
		Control	−4.82	2.33	0.12	−10.44	0.79
	Control	**dlPFC**	10.68	3.94	0.02	1.19	20.18
		non-dlPFC	4.82	2.33	0.12	−0.79	10.44
Latent working memory	**dlPFC**	**non-dlPFC**	−7.70	3.56	0.09	−16.29	0.89
		Control	−13.58	3.89	0.00	−22.97	−4.18
	Non-dlPFC	**dlPFC**	7.70	3.56	0.09	−0.89	16.29
		Control	−5.87	2.30	0.03	−11.43	−0.32
	Control	**dlPFC**	13.58	3.89	0.00	4.18	22.97
		non-dlPFC	5.87	2.30	0.03	0.32	11.43
Latent processing speed	**dlPFC**	**non-dlPFC**	−6.65	3.52	0.18	−15.13	1.84
		Control	−14.85	3.84	0.00	−24.12	−5.58
	Non-dlPFC	**dlPFC**	6.65	3.52	0.18	−1.84	15.13
		Control	−8.20	2.27	0.00	−13.69	−2.72
	Control	**dlPFC**	14.85	3.84	0.00	5.58	24.12
		non-dlPFC	8.20	2.27	0.00	2.72	13.69
Latent executive function	**dlPFC**	**non-dlPFC**	−7.99	3.56	0.08	−16.59	0.60
		Control	−13.60	3.90	0.00	−23.00	−4.20
	Non-dlPFC	**dlPFC**	7.99	3.56	0.08	−0.60	16.59
		Control	−5.61	2.30	0.05	−11.16	−0.05
	Control	**dlPFC**	13.60	3.90	0.00	4.20	23.00
		non-dlPFC	5.61	2.30	0.05	0.05	11.16

($n=55$), followed by Tukey's honestly significant difference (HSD) test to determine significant between-group differences ($p<0.01$, Bonferroni corrected).

3. Results

3.1. Structural equation modeling (SEM)

Fig. 2 shows SEM results. The fit for this model was appropriate: χ^2 (148)=322.65; CMIN/DF=2.2; RMSEA=0.072, CFI=0.91. Values depicted in Fig. 2 show that, at the latent variable level, the general factor of intelligence (*g*) and the executive function latent factor are near perfectly related ($r=1.0$). Nevertheless, it must be noted that (a) verbal comprehension, perceptual organization, working memory, and processing speed do show uniqueness, and (b) this uniqueness is also observed for the specific executive measures. Therefore, it is relevant to compare the three groups of participants both at the latent variable level and at the specific level (Colom & Thompson, 2011; Gläscher et al., 2010).

It is important to have empirical evidence regarding a proper generalization of the tested SEM model to the three groups of interest. This would validate the comparison made among groups. However, testing SEM models separately for controls, non-dlPFC patients, and dlPFC patients cannot be done because of sample size limitations. Therefore, we made three additional analyses: (a) excluding dlPFC patients ($n=207$), (b) excluding controls ($n=171$), and (c) excluding non-dlPFC patients ($n=71$). Obtained regression weights and fit indices were largely comparable to

Table 3
Descriptive statistics for measures of general intelligence and executive function with *g* removed.

Descriptives	Group	*N*	Mean	SD
Verbal comprehension removing *g*	**dlPFC**	19	102.82	20.30
	Non-dlPFC	152	100.52	14.77
	Control	55	97.59	13.44
Perceptual organization removing g	**dlPFC**	19	103.66	10.43
	Non-dlPFC	152	99.89	15.74
	Control	55	99.05	14.24
Working memory removing g	**dlPFC**	19	98.27	16.57
	Non-dlPFC	152	99.64	15.42
	Control	55	101.60	13.31
Processing speed removing *g*	**dlPFC**	19	100.20	16.69
	Non-dlPFC	152	97.71	14.74
	Control	55	106.25	13.52
Trail making test removing *g*	**dlPFC**	19	99.52	13.40
	Non-dlPFC	152	99.39	15.55
	Control	55	101.86	14.03
Verbal fluency test removing g	**dlPFC**	19	100.11	16.44
	Non-dlPFC	152	100.27	14.92
	Control	55	99.21	14.96
Card sorting test removing *g*	**dlPFC**	19	98.24	13.64
	Non-dlPFC	152	101.88	15.33
	Control	55	95.40	13.62
Twenty questions test removing g	**dlPFC**	19	93.44	14.24
	Non-dlPFC	152	101.36	14.03
	Control	55	98.52	17.23
Tower test removing *g*	**dlPFC**	19	102.68	17.14
	Non-dlPFC	152	100.06	14.74
	Control	55	98.91	15.11

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those values obtained for the complete dataset, which validates the comparisons made at the construct level.

3.2. Intelligence

Dorsolateral PFC lesion patients demonstrated significant deficits in the general factor of intelligence, *g* (Tables 1 and 2). This patient sample consistently obtained the lowest numeric levels of performance among groups tested on the WAIS, with significant deficits in *Working Memory* and *Processing Speed* (Table 2). The observed pattern of deficits highlights the importance of dlPFC for intelligence, supporting key competencies for working memory and mechanisms for the coordination of visual and motor representations underlying goal-directed behavior. However, when the influence of the general factor of intelligence (*g*) is removed from the first-order factors assessed by the WAIS, the deficits observed for the dlPFC patients in working memory and processing speed are no longer present (Tables 3 and 4). This pattern of findings suggests that the dlPFC plays a central role in the general factor of intelligence (*g*), rather than selectively mediating key competencies for working memory or processing speed.

We also observed reliable deficits in the non-dlPFC comparison group on tests of processing speed (Tables 1 and 2). Although this patient group was not the focus of our investigation and was constructed as a matched comparison group, we note that the observed deficits in processing speed likely originate from damage within the orbitofrontal cortex (see Supplemental Fig. 1; Barbey, Koenigs, and Grafman, 2011). A large body of neuroscience evidence indicates that the orbitofrontal cortex is responsible for the coordination and synthesis of visual and motor representations and appears to be important for performance on tests of processing speed (for a review, see Kringelbach, 2005).

3.3. Executive function

Patients with dlPFC damage also showed significantly worse performance than controls on the executive function latent factor, as well as on three out of five executive measures (trail, sorting, and twenty). However, when the effect of the general factor of intelligence (*g*) is removed from the specific executive measures, there is no longer a significant difference between dlPFC patients and controls (Tables 3 and 4). The overall absence of impairment suggests that the dlPFC is not functionally dedicated to support specific executive processes but may instead support higher-level mechanisms for general intelligence.

4. Discussion

The aim of the present investigation was to assess the role of the dlPFC in key competencies of general intelligence and executive function, examining whether this region (i) provides an integrative architecture for general intelligence or instead (ii) mediates a specific class of cognitive operations necessary for a particular domain of higher cognition. Using a relatively large sample of patients with dlPFC damage and a wide-ranging assessment of cognitive function, we report several main findings.

First, dlPFC lesions were reliably associated with deficits in general intelligence (*g*), with noteworthy impairment on measures of working memory and processing speed (see also, Barbey et al., in press b). These findings suggest that the dlPFC is necessary for intelligence, supporting key competencies for working memory and mechanisms for the coordination of visual and motor representations underlying goal-directed behavior. The recognized role of these processes in fluid intelligence further supports the neuroscience literature indicating that the dlPFC is particularly important for fluid aspects of intelligent behavior (see Blair, 2006; Woolgar et al., 2010).

Second, although dlPFC patients demonstrated the lowest levels of performance among groups tested on the D-KEFS, no reliable deficits were observed when the contribution of general intelligence (*g*) was removed. This pattern of findings suggests that the dlPFC is not functionally specialized for a specific executive function within the D-KEFS, but instead supports higher-level mechanisms for general intelligence.

Third, SEM results revealed the psychological structure of general intelligence and executive function—providing evidence that, at the latent variable level, these constructs are near perfectly correlated and further suggesting that high-level

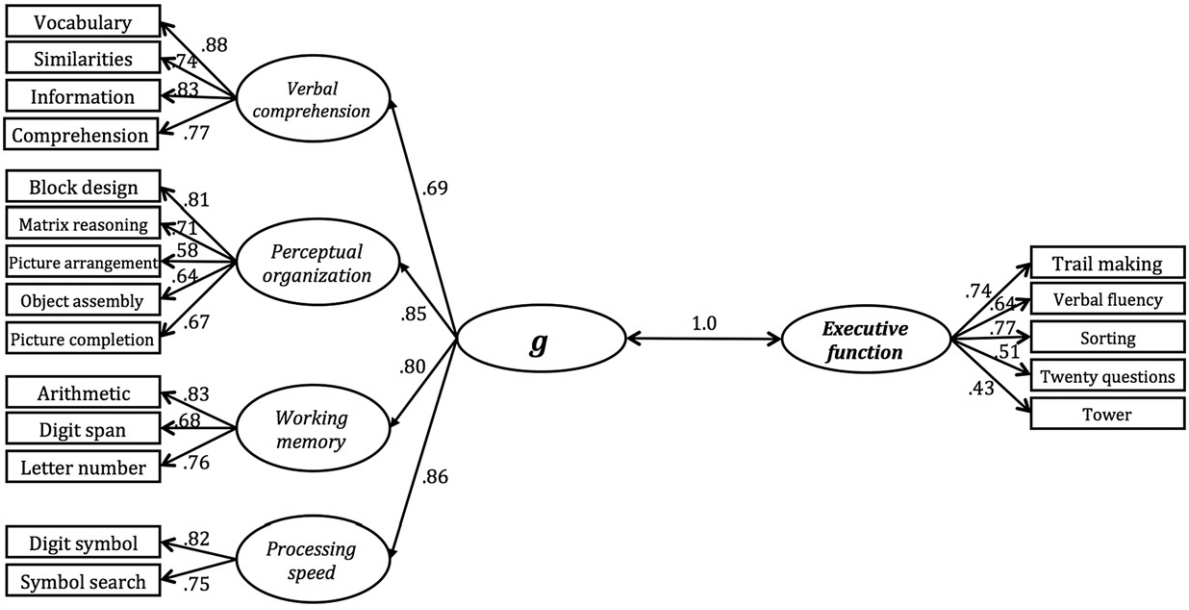

Fig. 2. SEM analysis of the administered WAIS and D-KEFS measures.

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Table 4
Inferential statistics for measures of general intelligence and executive function with *g* removed.

Bonferroni	(I) Group	(J) Group	Mean difference (I–J)	Standard error	Sig.	Confidence interval 95%	
						Upper limit	Lower limit
Verbal comprehension removing *g*	**dlPFC**	**Non-dlPFC**	2.30	3.65	1.00	−6.50	11.10
		Control	5.23	3.99	0.57	−4.40	14.85
	Non-dlPFC	**dlPFC**	−2.30	3.65	1.00	−11.10	6.50
		Control	2.93	2.36	0.65	−2.76	8.62
	Control	**dlPFC**	−5.23	3.99	0.57	−14.85	4.40
		Non-dlPFC	−2.93	2.36	0.65	−8.62	2.76
Perceptual organization removing *g*	**dlPFC**	**Non-dlPFC**	3.77	3.66	0.91	−5.04	12.59
		Control	4.61	4.00	0.75	−5.04	14.25
	Non-dlPFC	**dlPFC**	−3.77	3.66	0.91	−12.59	5.04
		Control	0.83	2.36	1.00	−4.87	6.54
	Control	**dlPFC**	−4.61	4.00	0.75	−14.25	5.04
		non-dlPFC	−0.83	2.36	1.00	−6.54	4.87
Working memory removing *g*	**dlPFC**	**non-dlPFC**	−1.37	3.66	1.00	−10.20	7.45
		Control	−3.34	4.00	1.00	−12.99	6.31
	Non-dlPFC	**dlPFC**	1.37	3.66	1.00	−7.45	10.20
		Control	−1.97	2.37	1.00	−7.67	3.74
	Control	**dlPFC**	3.34	4.00	1.00	−6.31	12.99
		non-dlPFC	1.97	2.37	1.00	−3.74	7.67
Processing speed removing *g*	**dlPFC**	**non-dlPFC**	2.49	3.56	1.00	−6.09	11.07
		Control	−6.05	3.89	0.37	−15.43	3.34
	Non-dlPFC	**dlPFC**	−2.49	3.56	1.00	−11.07	6.09
		Control	−8.53	2.30	0.00	−14.09	−2.98
	Control	**dlPFC**	6.05	3.89	0.37	−3.34	15.43
		non-dlPFC	8.53	2.30	0.00	2.98	14.09
Trail making test removing *g*	**dlPFC**	**non-dlPFC**	0.14	3.66	1.00	−8.69	8.96
		Control	−2.34	4.00	1.00	−11.99	7.30
	Non-dlPFC	**dlPFC**	−0.14	3.66	1.00	−8.96	8.69
		Control	−2.48	2.36	0.89	−8.18	3.23
	Control	**dlPFC**	2.34	4.00	1.00	−7.30	11.99
		non-dlPFC	2.48	2.36	0.89	−3.23	8.18
Verbal fluency test removing *g*	**dlPFC**	**non-dlPFC**	−0.17	3.66	1.00	−9.01	8.67
		Control	0.90	4.01	1.00	−8.77	10.57
	Non-dlPFC	**dlPFC**	0.17	3.66	1.00	−8.67	9.01
		Control	1.07	2.37	1.00	−4.65	6.78
	Control	**dlPFC**	−0.90	4.01	1.00	−10.57	8.77
		non-dlPFC	−1.07	2.37	1.00	−6.78	4.65
Card sorting test removing *g*	**dlPFC**	**non-dlPFC**	−3.64	3.60	0.94	−12.33	5.05
		Control	2.84	3.94	1.00	−6.66	12.34
	Non-dlPFC	**dlPFC**	3.64	3.60	0.94	−5.05	12.33
		Control	6.48	2.33	0.02	0.86	12.10
	Control	**dlPFC**	−2.84	3.94	1.00	−12.34	6.66
		non-dlPFC	−6.48	2.33	0.02	−12.10	−0.86
Twenty questions test removing *g*	**dlPFC**	**non-dlPFC**	−7.91	3.62	0.09	−16.65	0.82
		Control	−5.08	3.96	0.60	−14.63	4.48
	Non-dlPFC	**dlPFC**	7.91	3.62	0.09	−0.82	16.65
		Control	2.83	2.34	0.68	−2.82	8.48
	Control	**dlPFC**	5.08	3.96	0.60	−4.48	14.63
		non-dlPFC	−2.83	2.34	0.68	−8.48	2.82
Tower test removing *g*	**dlPFC**	**non-dlPFC**	2.62	3.66	1.00	−6.21	11.45
		Control	3.77	4.00	1.00	−5.89	13.42
	Non-dlPFC	**dlPFC**	−2.62	3.66	1.00	−11.45	6.21
		Control	1.14	2.37	1.00	−4.56	6.85
	Control	**dlPFC**	−3.77	4.00	1.00	−13.42	5.89
		non-dlPFC	−1.14	2.37	1.00	−6.85	4.56

cognition is supported by a domain-general information processing architecture.

Taken together, these findings help to elucidate the cognitive and neural architecture of higher cognition in the dlPFC, supporting the view that this region provides an integrative domain-general architecture for human intelligence rather than selectively mediating specific executive functions. This conclusion is supported by extensive neuroscience data implicating the dlPFC in general intelligence (Barbey et al., 2012; Deary et al., 2010). Rather than provide evidence for the involvement of the dlPFC in specific executive functions, this research demonstrates substantial adaptability of function (for reviews, see Miller, 2000; Miller & Cohen, 2001). The findings reported here, together with the emerging neuroscience literature, suggest that (1) the dlPFC has more than one function (Duncan et al., 2000; Duncan, 2010) and (2) functions of distinct cortical areas might overlap with one another to support an integrative architecture (Barbey et al., 2012; Jung & Haier, 2007).

According to this approach, neural computations should not be thought of as implemented by an individual area, but rather by the interaction among multiple areas. Specific brain regions are thought to belong to several intersecting networks based on their structural topology and functional connectivity (Passingham, Stephan, & Kotter, 2002). The impact of a brain region on behavior therefore depends on its structural and functional connectivity as a member of a broader information processing network.

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Recent advances in network theory have shown that regions characterized by a high degree of functional connectivity are important in regulating the flow and integration of information among areas (Guimera & Nunes Amaral, 2005; Guimera, Sales-Pardo, & Amaral, 2007; Sporns, Honey, & Kotter, 2007). Research indicates that the dlPFC is particularly important for linking multiple functional clusters, supporting an integrative architecture for the coordination of multiple brain systems (Sporns et al., 2007).

A growing body of evidence further indicates that this integrative architecture centrally depends on white matter fiber tracts that synthesize information across a broadly distributed neural system. A seminal model of general intelligence, the *Parieto-Frontal Integration Theory* (Jung & Haier, 2007), postulates central roles for cortical regions in the prefrontal (Brodmann areas 6, 9–10, 45–47), parietal (areas 7, 39–40), occipital (areas 18–19), and temporal association cortex (areas 21, 37). Recent voxel-based lesion-symptom mapping studies have sharpened our understanding of the role of white matter fiber tracts in binding these areas into an integrated system subserving *g* (Barbey, Krueger, & Grafman, in press; Gläscher et al., 2010, 2009; see also Rudrauf, Mehta, & Grabowski, 2008). Barbey et al. (2012) showed that the neural architecture of *g* is remarkably circumscribed, concentrated within the core of white matter fiber tracts that connect ventrolateral and dorsolateral PFC with the inferior parietal cortex and that terminate in the superior parietal lobule. Converging evidence is provided by Chiang et al. (2009), who report significant correlations between integrity of the superior fronto-occipital fasciculus and neuropsychological measures of general intelligence. The observed reliance upon white matter fiber tracts suggests that general intelligence is supported by the interregional communication among many brain areas, emphasizing the central role of the dlPFC and parietal cortex (Jung & Haier, 2007).

In designing the current study, we chose to contrast dlPFC patients with a demographically matched brain-damaged comparison sample. The matching was successful and the brain-damaged comparison group was highly similar on demographic variables (age, sex, years of education), pre- and post-combat measures of cognitive function, and lesion size. The selection of patient groups based on anatomically defined lesions in the present study is distinct from previous studies that have traditionally selected patients on the basis of their behavioral profile (e.g., Shallice & Vallar, 1990). An anatomically defined approach can support stronger inferences about brain-behavior relationships by examining the causal contribution of a specific brain region to general intelligence and executive function rather than indirectly inferring these mechanisms from a particular behavioral profile (cf. Baldo & Dronkers, 2006). This design helps to isolate scientifically the causal contribution of dlPFC damage to specific higher cognitive functions. The observed pattern of significant between-group differences on general intelligence provides strong evidence that dlPFC damage leads to disproportionate defects in intelligence, relative to damage outside the dlPFC. Conversely, the reliable lack of significant between-group differences on tests of executive function (with *g* removed) provides key evidence that dlPFC damage, per se, does not lead to deficits in executive function.

The reported findings have significant implications for the neuropsychological assessment of brain-injured patients. From a clinical perspective, understanding general intelligence deficits in patients with dlPFC lesions may facilitate the design of appropriate assessment tools and rehabilitation strategies, with potential improvement in patients' cognitive abilities and daily living. These data show that impairments at the level of verbal and performance IQ (Tables 1 and 2), or on specific measures of executive function (Tables 3 and 4), are not necessarily caused by dlPFC damage. Diagnostic evidence for the preserved functioning of the dlPFC instead derived from performance at the highest level, on global tests of general intelligence (*g*) representing key competencies for working memory and processing speed (Tables 1 and 2). These findings highlight specific tests of the WAIS that may be targeted in clinical investigations to assess the functioning of dlPFC (Blair, 2006).

It is important to emphasize in closing that the abilities measured by the WAIS and D-KEFS do not provide a comprehensive assessment of all human cognitive abilities. There are other aspects of human intelligence in addition to those abilities measured by the WAIS and D-KEFS that contribute to mental life, notably those related to social and emotional functioning (for evidence supporting the involvement of the dlPFC in emotional intelligence, (see, Barbey et al. 2009a; Krueger et al., 2009). We stress that the conclusions of our study speak only to the necessity of the dlPFC, not the entire network of structures that participate. Understanding the neural architecture of human intelligence and executive functions will ultimately require knowledge of the entire network, the contributions made by each of the components, and the role of white matter fiber tracts that communicate and synthesize information between them. The results reported here contribute to this emerging research program by helping to elucidate the involvement of the dlPFC, indicating that this region is necessary for global aspects of general intelligence rather than selectively mediating specific executive functions.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at http://dx.doi.org/10.1016/j.neuropsychologia.2012.05.017.

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