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Neural correlates of "analytical-specific visual perception" and degree of task difficulty as investigated by the Mangina-Test: A functional magnetic resonance imaging (fMRI) study in young healthy adults

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ABSTRACT

The Mangina-Test is a neuropsychometric method for evaluating varying degrees of "analytical-specific perception" as they relate to learning abilities and disabilities. It consists of the identification of simple stimuli which are masked within a complex configuration according to their exact size, dimension, direction, spatial orientation, and shape within a limited span of time. This test has been successfully applied in clinical settings for the assessment of cognitive abilities and disorders in young and elderly populations. This investigation aimed to examine the neural correlates of analytical-specific visual perceptual processes as measured by the Mangina-Test.

Functional Magnetic Resonance Imaging (fMRI) was recorded during the administration of a computer-adapted version of the Mangina-Test in twelve young healthy adults. Multiple linear regression analysis was applied to estimate the overall brain activation during task accomplishment. In addition, the fMRI response area was correlated with task difficulty, in order to explore the spatial distribution of brain regions modulated by increasing task demand.

Results indicate that a widely distributed bilateral network of brain regions, including the ventral and dorsal occipital cortex, parietal lobule, frontal and supplementary eye field, dorsolateral prefrontal cortex, and supplementary motor area, was significantly activated during test performance. Moreover, increasing difficulty significantly enhanced the neural response of ventral and dorsal occipital regions, frontal eye field, and superior parietal sulcus bilaterally, as well as the right dorsolateral prefrontal cortex. Conversely, neural activity in the left temporo-parietal junction, inferior frontal gyrus, and bilateral middle-superior temporal cortex was inversely correlated with task difficulty. Results also indicate that performance in the Mangina-Test requires an optimal integration between the enhancement of activity in specific task-related cortical areas and suppression of interfering noise from unrelated brain regions.

1. Introduction

Subtle learning disabilities are frequently encountered within the general population and often misdiagnosed as being motivational or emotional in origin. Accurate detection of the degree of learning skills represents a major challenge in Cognitive Psychophysiology and behavioral sciences. Learning disabilities in children and adolescents have been associated with inadequate analytical-specific perceptual skills (Mangina, 1981, 1994a,b,c, 1998; Mangina and Beuzeron-Mangina, 1988, 1992a,b, 2004a,b; Mangina and Sokolov, 2006; Mangina et al., 1998, 2000). The Mangina-Test proved to successfully measure varying degrees of analytical-specific perceptual learning abilities and disabilities (Mangina, 1981, 1994a,b,c, 1998). One of the theoretical basis of the Mangina-Test is that "analytical-specific visual perception" goes beyond simple sensory perception by engaging complex cognitive analysis of subtle perceptual relationships of exact similarities and differences within a complex configuration of stimuli in limited span of time. The adequate development of these functions relies on the ability of neuronal networks to integrate sensory–motor–cognitive information through multiple cortico-cortical and cortico-limbic synaptic interconnections.

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The Mangina-Test consists in the discrimination of simple stimuli inserted in other increasingly more complex stimuli according to their exact direction, spatial orientation, size, dimension and shape in a limited span of time. Since these geometrical properties are preferentially related to either mathematical abilities or abilities in reading and reading comprehension, the Mangina-Test allows to distinguish difficulties in mathematics and/or reading /comprehension that are caused by learning disorders, in addition to measuring varying degrees of learning abilities and disabilities in general. Furthermore, the test is non-verbal and culture-free, thus, being suitable for administration to children and for international use without any modification, and is independent of general intelligence and gender variables (Mangina, 1981, 1994a,b,c, 1998).

The Mangina-Test has been applied in conjunction with topographic mapping of event-related brain potentials and bilateral electrodermal activity to highlight the neurophysiological indicants of learning and attentional disorders with concomitant severe behavioral problems (Mangina and Beuzeron-Mangina, 1988, 1992a,b; Mangina et al., 1998, 2000; Mangina and Beuzeron-Mangina, 2004a,b; Mangina and Sokolov, 2006). In addition, neurophysiological markers along with the use of the Mangina-Test have been found to differentiate and describe "pure" attention deficit hyperactivity disorder (ADHD), comorbid ADHD with learning disabilities, "pure" learning disabled and normals (Mangina and Beuzeron-Mangina, 2006, 2008, 2009–this issue). Significantly impaired Mangina-Test performance along with event-related brain potential irregularities has been reported in patients afflicted with Early Alzheimer's Disease as compared to age-matched normal controls (Beuzeron-Mangina and Mangina, 1998, 2000). This is in line with the well-known correlation between cognitive decline and early degeneration of limbic structures followed by progressive alterations of the associative neocortical areas (Nagy et al., 1999a,b). Other clinical applications of the Mangina-Test include children and adolescents with neuropsychiatric pathologies and language impairments (Chiarenza and Benvenuti, 2002; Chiarenza et al., 2006), neuropsychometric evaluation of ADHD (Karakaş et al., 2006) and differentiation of ADHD and learning disabilities (Karakaş et al., 2008).

Although the Mangina-Test is widely applied for the diagnosis of varying degrees of learning abilities and disabilities, the neuronal networks specifically activated during the performance of this test require further exploration and elaboration. The Mangina-Test has the distinct advantage of eliciting specific analytical perceptual processes with relevance to cognitive ability or disorders. At the same time, it shares some common characteristics with more general visual search tasks involving exploration of the visual field by eye movements, attentional shifts and comparison of visual features. Other studies have reported significant interaction between frontal eye field and posterior parietal cortex for successful accomplishment of visual search tasks (Müller et al., 2003; Egner et al., 2008; Kalla et al., 2008). In addition, activation of these cortical areas is disrupted in patients with cognitive impairments such as Alzheimer's dementia (Hao et al., 2005).

The present research aimed at investigating the neural correlates of analytical-specific visual perceptual processes as measured by the Mangina-Test by applying functional magnetic resonance imaging (fMRI). In particular, the goals of this experimental design were the exploration of the spatial distribution of neuronal networks engaged by the Mangina-Test stimuli in addition to investigating as to whether the degree of difficulty of these stimuli modulates neural activity.

2. Materials and methods

2.1. Participants

Twelve healthy right-handed volunteers (six females, mean age $\pm$ S.D. $= 26 \pm 3$ years) participated in the experiment. Clinical examinations and laboratory tests were administered to rule out history or presence of any relevant medical, neurological or psychiatric disorder, and use of substance that could affect brain function or metabolism. All were free of medication including over the counter medication.

2.2. Ethics

Written informed consent to participation was obtained from all volunteer participants after detailed explanation of the study procedures and risks involved. The entire research protocol was approved by the Research Ethics Board of the University.

2.3. Experimental design

The experimental design faithfully reproduced the original psychophysical paper-and-pencil version of the Mangina-Test (Mangina, 1981, 1994a,b,c, 1998). This test is composed of 44 simple and 44 complex original geometrical visual stimuli, presented with an increasing degree of difficulty (Fig. 1a). One simple and one complex stimulus are presented simultaneously. The task consists of exactly identifying

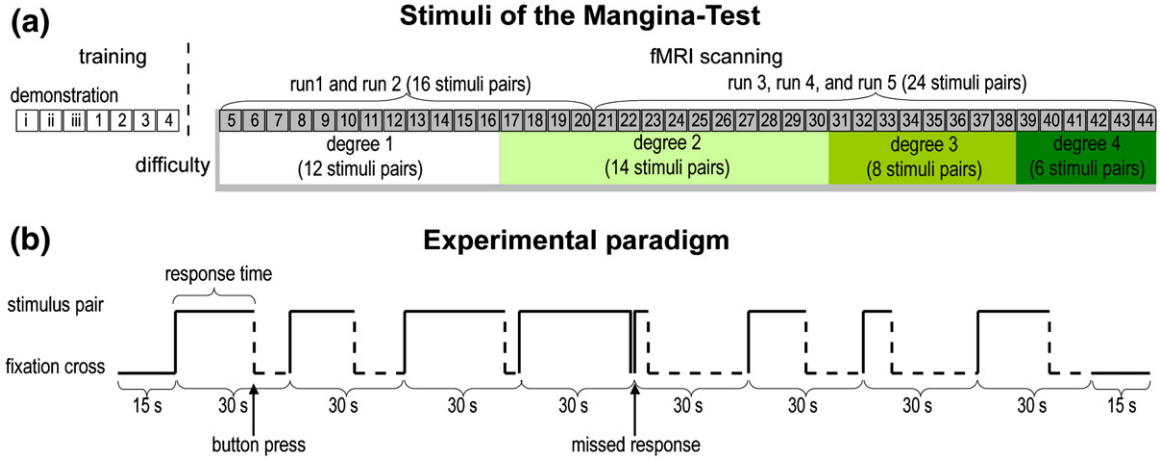

Fig. 1. a) Stimuli of the Mangina-Test. Three demonstration stimuli pairs and the first 4 stimuli pairs of the test were used for training subjects out of the magnet, while the last 40 were presented during fMRI scanning. Stimuli pairs between 5–20 were randomly presented in runs 1 and 2, while stimuli pairs between 21–44 were randomly presented in runs 3, 4, and 5. According to difficulty, stimuli pairs were classified into four subgroups, from the most easy degree 1 including 5–16 stimuli pairs (white color, least difficult), to the average difficult degrees 2 and 3, respectively including 17–30 stimuli pairs (light green) and 31–38 stimuli pairs (green), to the most difficult degree 4 including 39–44 stimuli pairs (dark green). b) Experimental paradigm. Each functional run began and ended with 15 s rest and contained 8 stimuli pairs, presented every 30 s. Subjects had to press a button upon identification of the simple stimulus within the complex stimulus. After button press the stimulus pair was replaced by a fixation cross (rest). In case of missed responses within 30 s, the next stimulus pair would immediately follow without resting period.

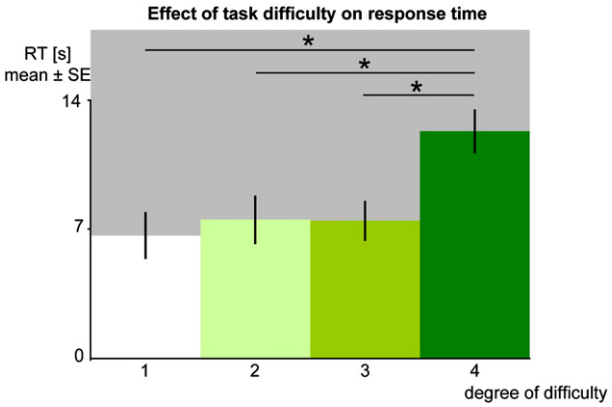

Fig. 2. Effect of task difficulty on response time. ANOVA showed that RT was significantly modulated by task difficulty ($F(3)$: $P<0.005$). Post-hoc t-test analysis with Bonferroni correction indicated that RT of the stimuli pairs with degree of difficulty 4 (most difficult) was significantly longer than RT of the stimuli pairs with degree of difficulty 3, 2, and 1 (increasingly easier). SE = standard error; *Bonferroni-corrected $P<0.05$.

and tracing completely with a fine marker the simple stimulus which is masked within a complex configuration of stimuli varying in direction, spatial orientation, size, dimension, and shape in a limited span of time. A computer-adapted version was specifically developed for the purpose of applying it during fMRI and was controlled by using Presentation® (Version 9.80, http://www.neurobs.com). The paper-and-pencil version of the test was administered to all subjects immediately after scanning, in order to counter-check the correct responses given during the fMRI session and to measure their individual analytical-specific perceptual skills. Before fMRI recording, subjects were informed about all the experimental procedures and were allowed to familiarize with the task using some demonstration stimuli and the first four stimuli pairs of the test. The last 40 stimuli pairs of the Mangina-Test were selected for presentation during the fMRI session which consisted of five runs. Each run contained 8 stimuli pairs and lasted 4 min 30 s, including 15 s rest at the beginning and the end of the stimulation block (Fig. 1b). Subjects were instructed to carefully look at the stimuli, to mentally identify the simple stimulus within the complex configuration, and to press a button with their right hand when being confident of successful identification. Stimuli pairs were presented every 30 s and were replaced by a fixation cross following button press. Therefore, stimulus duration was self-paced by the subjects being examined and corresponded exactly to the time spent for the identification of the simple stimulus within the complex one, i.e. response time (RT). Stimuli pairs 5–20 of the Mangina-Test were randomly presented in the first two runs and stimuli pairs 21–44 were randomly presented in the last three runs (Fig. 1a). This stimulus ordering ensured a certain degree of increasing difficulty between the beginning and the end of the recording session, while allowing for randomized inter-individual stimulus presentation which is highly beneficial for fMRI statistical analysis.

2.4. fMRI recording

Multi-slice axial echo-planar images (EPIs) were acquired on a 1.5 T MRI scanner (GE Medical Systems Signa) with TE = 40 ms, TR = 2.5 s, flip angle 90°, FOV = 240 mm with 64×64 acquisition matrix (3.75 mm×3.75 mm in-plane resolution) and 33 contiguous 4-mm slices. Each functional run consisted of 112 brain volumes and the first four (dummy volumes) were discarded from analysis. Head movements were limited by carefully placed constraints. Stimuli were projected onto a screen located near the bottom of the bore and viewed from a mirror mounted on the head coil. A high resolution T_1-weighted spoiled grass structural scan was acquired at the beginning of the recording session (TE = 3.58 ms, TR = 19.58 ms, flip angle 10°, FOV = 240 mm with 0.469×0.469 mm in-plane resolution, 512×512 acquisition matrix, and 1 mm axial slice thickness).

2.5. Behavioral analysis

Analysis of variance (ANOVA) and post-hoc t-tests with Bonferroni correction were applied to evaluate the modulation of response time by the degree of difficulty of the stimuli pairs of the Mangina-Test.

2.6. fMRI analysis

Structural and functional images were analyzed with the AFNI software (Analysis of Functional NeuroImages, http://afni.nimh.nih.gov/afni, Cox (1996)). Prior to statistical analysis, single-subject fMRI data were pre-processed by slice timing and rigid head movements correction, spatial smoothing with isotropic Gaussian filter ($\sigma = 3$ mm), and global mean intensity normalization to calculate the percentage of signal change.

Subsequently, functional images time series ($Y(t)$) at each voxel v was fitted by least squares method to a multiple linear regression model that included regressors of interest as well as confounds (Eq. (1)).

$$Y_v(t) = \sum_{s=1}^{40} \beta_{v,s} \cdot X_s(t) + \sum_{r=1}^{5} \left[a_{v,r} + b_{v,r} \cdot t + c_{v,r} \cdot t^2 \right] + \sum_{p=1}^{6} m_{v,p} \cdot M_{v,p}(t) + \text{noise}_v(t). \quad (1)$$

Confounds consisted of a different quadratic baseline for each run r and of three-rotation and three-translation rigid head motion parameters ($M(t)$) concatenated across runs and estimated from images preprocessing. Each stimulus s of the Mangina-Test was modeled with a separate regressor of interest ($X(t)$), obtained by convolving a square wave of duration corresponding to response time (RT_s) with a gamma variate function (Cohen (1997) — peak value 1 at $t = 4$) that represented the impulse hemodynamic response (HRF) (http://afni.nimh.nih.gov/afni/doc/faq/17). As a result, apart from coefficients of no-interest (a, b, c, and m), this method provided 40 stimulus-specific β-weights for all subjects, accounting for individual response time to each stimulus pair of the Mangina-Test.

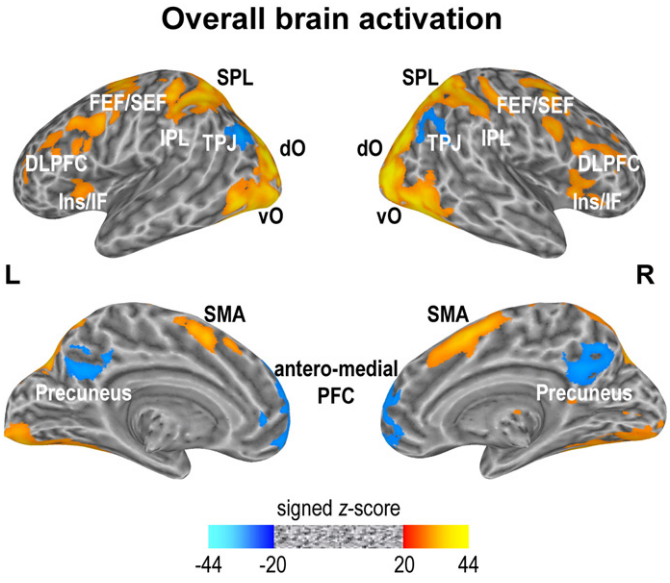

Fig. 3. Overall brain activation. Spatial distribution of the overall brain response to the stimuli pairs of the Mangina-Test. Significant functional activations are depicted according to signed z-score, i.e. accounting for the sign of the average of all regression coefficients of interest in each voxel ($z>20$). Color-coded statistics are depicted on the lateral (top) and medial (bottom) surfaces of a standard inflated brain. L = left, R = right hemisphere; dO = dorsal, vO = ventral occipital cortex; TPJ = temporo-parietal junction; IPL = inferior, SPL = superior parietal lobule, FEF = frontal, SEF = supplementary eye field; DLPFC = dorsolateral, PFC = prefrontal cortex; Ins = insula; IF = inferior frontal cortex; SMA = supplementary motor area.

Table 1
Overall activation: mean signed *z*-score and local maxima coordinates (Talairach and Tournoux, 1988) of clusters of significantly engaged voxels in the overall group activation map.

Brain areas		BA	H	Overall activation				Effect of difficulty			
				z-score	*x*	*y*	*z*	$\rho_{\bullet,2}$	*x*	*y*	*z*
Occipital	Ventral	19/37	L	29.4	-27	-86	2	0.42	-20	-78	-17
			R	28.3	35	-81	2	0.49	29	-73	-15
	Dorsal	18/19	L	28.8	-28	-82	10	0.45	-13	-94	12
			R	27.8	31	-75	20	0.38	17	-89	14
Parietal	IPL	40	L	27.7	-37	-48	48				
			R	25.7	32	-57	47				
	SPL	7	L	28.3	-18	-67	54	0.31	-17	-64	56
			R	29.1	24	-64	54	0.50	14	-76	52
	TPJ	19/39	L	-22.8	-44	-71	33	-0.33	-45	-71	37
			R	-21.7	49	-66	27				
	Precuneus	7/31	L/R	-22.5	1	-48	32				
Temporal	Middle-superior	21/22	L					-0.28	-60	-23	-4
			R					-0.34	66	-37	3
Frontal	FEF/SEF	6	L	24.3	-25	-14	54	0.30	-28	-11	63
			R	24.2	27	-10	52	0.27	26	-6	52
	SMA	6	L/R	24.8	2	2	50				
	DLPFC	9/46	L	24.5	-46	2	35				
			L	21.9	-40	24	29				
			R	23.9	51	3	39	0.34	47	2	27
			R					0.37	48	37	24
	Ins/IF	45/47	L	22.1	-28	19	8	-0.39	-41	26	-2
			R	23.2	34	18	7				
	Antero-medial PFC	9/10	L/R	-21.6	4	55	0				

Effect of difficulty: mean correlation coefficient between fMRI area and task difficulty and local maxima coordinates of clusters of voxels significantly modulated by task difficulty. BA = Brodmann's area; H = hemisphere, L = left, R = right; *z*-score = signed *z*-score, $\rho_{\bullet,2}$ = correlation coefficient between fMRI area and task difficulty; *x*,*y*,*z* = spatial coordinates in the Talairach and Tournoux atlas. IPL = inferior parietal lobule, SPL = superior parietal lobule; TPJ = temporo-parietal junction; FEF = frontal, SEF = supplementary eye field; SMA = supplementary motor area; DLPFC = dorsolateral prefrontal cortex; Ins = insula, IF = inferior frontal cortex.

After spatial warping into the Talairach and Tournoux atlas (1988) and resampling to 1 mm^3 voxels, random effect group analysis (second level analysis) was performed to account for inter-individual variance, using the appropriate individual statistical contrast images. Individual overall *F*-statistics were transformed to *z*-score, averaged across subjects, and scaled by the square root of the sample size for computing an overall group *z*-map. This map represented the global brain response to the stimuli pairs of the Mangina-Test (significance threshold $z>20$). The area (A) subtended by the fMRI response to each stimulus pair s was computed in each voxel v to measure the modulation of brain activity by task difficulty. However, A increases with stimulus duration, i.e. RT, and RT likely increases with task difficulty. Therefore, fMRI area was modeled as a linear function of response time (null hypothesis H_0): the specific contribution of task difficulty was estimated by asking to what extent adding a 4-degree difficulty parameter (D, see Fig. 1a) significantly improved the explanatory capabilities of the model (alternative hypothesis H_a) (Eq. (2)).

$$\begin{cases} H_0 : A_{v,s} = \rho_{v,0} + \rho_{v,1} \cdot RT_s + \text{noise}_v \\ H_a : A_{v,s} = \rho_{v,0} + \rho_{v,1} \cdot \text{RT}_s + \rho_{v,2} \cdot D_s + \text{noise}_v \end{cases}. \quad (2)$$

Significance of $\rho_{v,2}$ was assessed by *t*-test analysis and the false discovery rate (FDR) method was applied to correct for multiple comparisons (FDR-corrected $P<0.05$). Since time length, amplitude, and subtended area of the fMRI response are markedly influenced by stimulus duration, i.e., response time, the choice of considering RT while modeling the fMRI response area allowed to rule out the contribution of stimulus duration and to highlight the specific contribution of the level of difficulty to the subtended area.

3. Results

3.1. Behavioral results

All subjects were able to correctly accomplish the task and accuracy was generally high (36 ± 4 correct answers out of 40 items). Analysis of variance (ANOVA) showed that the interaction between RT and task difficulty was statistically significant ($F(3)$: $P<0.005$): in particular, the stimuli pairs with degree of difficulty 4 (most difficult) were characterized by significantly longer RT than all the other easier stimuli pairs (Bonferroni-corrected $P<0.05$) (Fig. 2).

3.2. Overall brain activation

During the Mangina-Test, a widely distributed bilateral network of brain regions was significantly engaged, including ventral and dorsal occipital regions, medial precuneus, temporo-parietal junction, inferior and superior parietal lobule, frontal/supplementary eye field, supplementary motor area, dorsolateral prefrontal cortex, inferior frontal gyrus/insula, and antero-medial prefrontal cortex (Fig. 3, Table 1).

3.3. Effect of task difficulty on brain activity

Neural response was significantly modulated by task difficulty in a highly specific network of brain regions on the lateral surface of both hemispheres. In particular, hemodynamic response area increased with task difficulty in the ventral and dorsal occipital cortex, inferior parietal lobule, and frontal eye field bilaterally, and in the right dorsolateral prefrontal cortex (Figs. 4 and 5, Table 1). Conversely, the fMRI response to stimuli pairs grouped by difficulty was always negative in several regions of the default mode system (Raichle and Snyder, 2007), namely, the left temporo-parietal junction and anterior inferior frontal gyrus, along with the middle-superior temporal gyrus bilaterally (Figs. 4 and 5, Table 1). In addition, the signed value of the fMRI area was negatively correlated with difficulty, meaning that the more difficult the subgroup of stimuli pairs, the more negative the fMRI response (Figs. 4 and 5, Table 1).

4. Discussion

This work investigated the neural basis of analytical-specific visual perceptual processes activated during the Mangina-Test. A widely

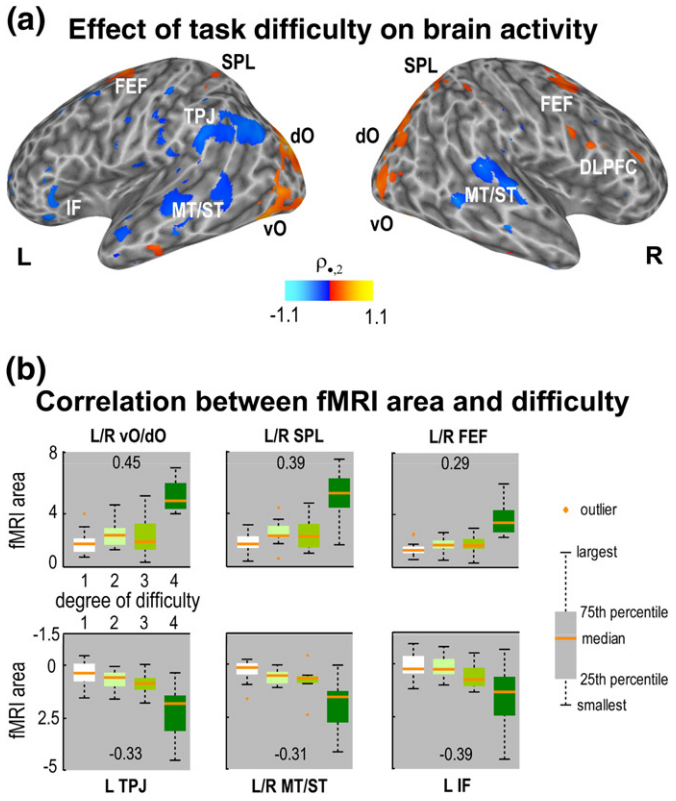

Fig. 4. a) Effect of task difficulty on brain activity. Spatial distribution of the brain regions where neural activity is significantly modulated by task difficulty (FDR-corrected $P<0.05$). Color-coded map of the regression coefficient between fMRI area and difficulty ($\rho_{\bullet,2}$) estimated by multiple linear regression (see fMRI analysis) is depicted on the lateral surfaces of a standard inflated brain (Talairach and Tournoux, 1988). b) Correlation between fMRI area and difficulty. Each panel shows the boxplot of the fMRI area averaged over a specific region of interest (ROIs) for the stimuli pairs of the Mangina-Test grouped by the degree of difficulty and the linear correlation value between fMRI area and difficulty. L = left, R = right hemisphere; dO = dorsal, vO = ventral occipital cortex; TPJ = temporo-parietal junction; SPL = superior parietal lobule; FEF = frontal eye field; DLPFC = dorsolateral prefrontal cortex; MT/ST = middle-superior temporal cortex; IF = inferior frontal cortex.

distributed bilateral network of brain regions, including the ventral and dorsal occipital cortex, parietal lobule, frontal and supplementary eye field, dorsolateral prefrontal cortex, and supplementary motor area, was significantly activated during test performance. In addition, increasing difficulty was associated with longer response time and significantly enhanced the neural response of ventral and dorsal occipital regions, frontal eye field, and superior parietal lobule bilaterally, and right dorsolateral prefrontal cortex. Conversely, neural activity in the left temporo-parietal junction, inferior frontal gyrus, and bilateral middle-superior temporal cortex was inversely correlated with task difficulty.

Behavioral results indicated that RT increased slightly with degree of difficulty 1 to 3 and then had a considerable and statistically significant step increment at degree 4. This finding suggests that the geometrical characteristics of the complex stimuli progressively complicate the identification of the masked simple stimuli up to a critical point, beyond which analytical-specific visual perceptual processes are maximally engaged up to their limits.

The striate and extrastriate visual cortex (vO and dO) were extensively activated by analytical-specific visual perceptual processes. Robust engagement of these regions had to be expected from the considerable importance of visual features of these tasks. Moreover, activity in these regions significantly increased with difficulty, suggesting that their functional role is essential for task performance, especially for highly demanding analytical visual perceptual processes.

fMRI response of the medial precuneus and anterior-medial PFC was negative as compared to baseline. Since these regions are part of the default mode system (Raichle and Snyder, 2007), their activation could actually be lesser during task performance than rest. However, further research is needed to clearly ascertain their role in the context of analytical-specific visual perceptual processes.

Speedy and exact identification of simple stimuli masked within complex configurations occurring during the Mangina-Test, requires multiple rapid saccades between the two stimuli. Indeed, the results of the present study showed a significant engagement of frontal and supplementary eye field structures: these regions have similar functional organization, are highly interconnected also with the superior culliculus, and are responsible for planning and controlling goal-directed eye movements (Russo and Bruce, 2000; Stuphorn et al., 2000). The parietal cortex has been implicated in attentional shift tasks, in conjunction with the frontal eye field structures (Culham et al., 1998; Egner et al., 2008). In line with these previous reports, the present study showed robust activation of a fronto-parietal network that likely exerts a leading control on saccadic eye movements, focused attention, and visuo-spatial comparison. More specifically, a recent study by Kalla et al. (2008) with double-pulse transcranial magnetic stimulation (TMS), has reported different timing of disruption of performance in the posterior parietal cortex and frontal eye field during a visual search task. These authors postulated that earlier involvement of FEF might denote greater influence on preparation of saccades, while later involvement of parietal cortex might better agree with visuomotor transformations.

Attentional processes have been extensively investigated in different conditions. A recent review by Corbetta et al. (2008) highlights the existence of two main systems of attending to environmental stimuli, i.e. a dorsal and a ventral fronto-parietal network. The dorsal network involves the superior parietal lobule and frontal eye field, while the ventral network engages the temporo-parietal junction and the inferior frontal gyrus. Interactions between these two pathways

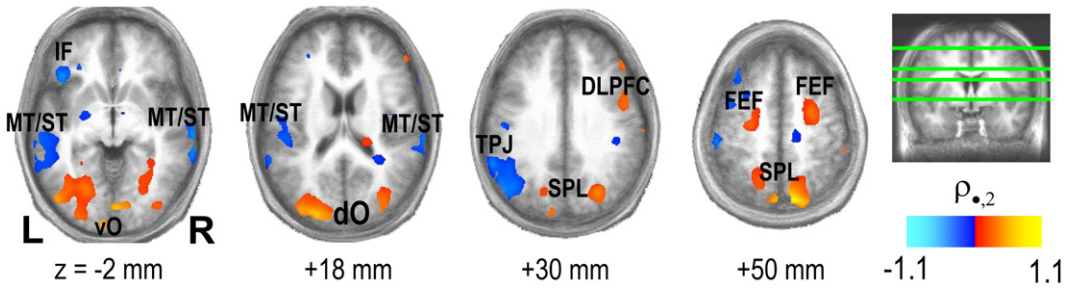

Fig. 5. Spatial distribution of the brain regions where neural activity is significantly modulated by task difficulty (FDR-corrected $P<0.05$). Color-coded map of the regression coefficient between fMRI area and difficulty ($\rho_{\bullet,2}$) estimated by multiple linear regression (see fMRI analysis) is depicted on four axial slices at $z=-2$, +18, +30, and +50 mm (Talairach and Tournoux, 1988). L = left, R = right hemisphere; dO = dorsal, vO = ventral occipital cortex; TPJ = temporo-parietal junction; SPL = superior parietal lobule; FEF = frontal eye field; DLPFC = dorsolateral prefrontal cortex; MT/ST = middle-superior temporal cortex; IF = inferior frontal cortex.

have been proposed as a functional basis of shifting attention towards salient stimuli (Corbetta and Shulman, 2002). Specifically, the contribution of the dorsal network has been mainly related to the top–down control of stimulus features and locations processed by sensory cortex. Activation of the ventral network has been observed during perception of irrelevant objects that are similar to targets (Serences et al., 2005). This finding supports the interpretation of reduced engagement of these regions with the increasing degree of difficulty of stimuli reported in our present investigation. In fact, as difficulty increases, task accomplishment requires subjects to focus their attention on highly specific geometrical features of simple and complex stimuli, thus preventing useless interference by mechanisms of reorienting attention to unimportant objects. Interestingly, in the present study, correlation between fMRI area and task difficulty resulted in a dissociation between direct proportionality in the right DLPFC and inverse proportionality in the left IFG. This behavior has been already reported in a PET study by Grady et al. (1996) during a match-to-sample task with degraded faces. Increased reliance on higher order cognitive functions located in the frontal cortex that likely intervene at later stages as compared to sensory visual processes, might account for the positive correlation between activation of the right DLPFC and task difficulty. In this region, modulation of neural activity by task difficulty has also been reported by other positron emission tomography (PET) and fMRI studies during visuo-spatial paired associates learning task (Gould et al., 2003), degraded face matching task (Grady et al., 1996; Bokde et al., 2005) and attentive tracking (Culham et al., 1998). Negative correlation with left IFG suggests that engagement of this region is not helpful for efficient task accomplishment. In addition, this lateralization of prefrontal activity, as visuo-spatial demand increases, matches the preferential activation of the right as compared to the left hemisphere in spatial tasks, such as spatial working memory (Jonides et al., 1993), object identification (Haxby et al., 1991), and global attention paradigms (Fink et al., 1996). Explanations for a right-lateralized modulation of DLPFC with task difficulty might be related to its role in general cognitive demand and spatial processing (Gould et al., 2003), coordination among other task-related areas and increased visual search time (Grady et al., 1996; Bokde et al., 2005).

Prefrontal and parietal regions play a key role for the top–down control of sensory–motor systems and memory functions. Disruption of these areas is related to severe pathological conditions in both young and elderly, such as ADHD, learning disabilities and Alzheimer's disease. Previous studies have highlighted the pertinence of neurophysiological recordings in depicting the neural basis of these functional alterations pertaining to the inhibitory, attentional and cognitive domains (Mangina et al., 1998, 2000; Mangina and Beuzeron-Mangina, 2004a, b; Beuzeron-Mangina and Mangina, 2000; Mangina and Sokolov, 2006; Hao et al., 2005). Furthermore, the application of neurophysiological methods in conjunction with the neuropsychometric assessment of "analytical-specific visual perception" provided by the Mangina-Test, have been proposed for the evaluation and treatment follow-up of pathological populations (Mangina and Beuzeron-Mangina, 1992a,b, 2004a,b; Beuzeron-Mangina and Mangina, 2000; Mangina et al., 2000; Mangina and Sokolov, 2006). The results presented in this study provide further evidence and quantitative indications about the usefulness of the Mangina-Test for the investigation of pathological alterations of fronto-parietal neuronal networks. Specifically, the integration of occipital, temporo-parietal, and frontal neuronal functions measured during the execution of the Mangina-Test along with the effects of task difficulty, shed new light on the neural basis of analytical-specific perceptual processing mechanisms and the relationship between developmental, attentional, cognitive and neurodegenerative impairments.

In conclusion, performance on the Mangina-Test requires the integration between enhancement of activity in specific task-related cortical areas and suppression of interfering noise from unrelated brain regions.

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