Modulation of specific brain activity by the perceptual analysis of very subtle geometrical relationships of the Mangina-Test stimuli: A functional magnetic resonance imaging (fMRI) investigation in young healthy adults

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ABSTRACT

The Mangina-Test provides a neuropsychometric assessment of varying degrees of “Analytical-Specific Visual Perception”, i.e., the ability to identify simple stimuli inserted into more complex ones according to their exact geometrical properties in a limited span of time. Perceptual analysis of stimuli dealing with the exact discrimination of size and dimension is related more to mathematical abilities (MATH), while perceptual analysis of direction and spatial orientation is related more to abilities in reading and reading comprehension (READ). Some stimuli are MIXED since they deal with both of the above features combined.

We previously determined the distributed neuronal network of analytical-specific visual perceptual processes as measured by the Mangina-Test. Here, we aim at further assessing as to how brain activity is differentially modulated by the discrimination of very subtle category-specific perceptual relationships. Brain activity was measured by functional magnetic resonance imaging in 12 young healthy subjects while they performed a computer-adapted version of the Mangina-Test.

Behavioral results of the present study indicate that performance was not different among stimulus categories. However, brain functional data show that analytical-specific perceptual processes for MATH, READ and MIXED stimuli rely on partially distinct brain circuits. Bilateral posterior parietal, premotor and prefrontal regions along with the anterior cingulate appeared to be more activated by MATH stimuli, while READ stimuli predominantly activated bilateral medial occipito-temporal, amygdala/parahippocampal and sensorimotor cortices, and the right inferior frontal cortex. Moreover, the posterior parahippocampal cortex showed a higher activity specifically for MIXED stimuli. Altogether, these findings demonstrate that in the Mangina-Test, the exact discrimination of very subtle perceptual relationships between geometrical stimuli distinctly modulates cerebral activity, so that category-specific brain responses can be related to identifiable cognitive abilities.

1. Introduction

One of the important aspects of the Mangina Diagnostic Tool of Visual Perception (Mangina-Test) is that it has been purposely constructed to measure perceptual analysis of specific stimuli dealing with size and dimension vs. direction and spatial orientation. It has been shown that in the Mangina-Test, the exact discrimination of stimuli varying in size and dimension are related more to mathematical abilities whereas, the precise detection of stimuli varying in direction and spatial orientation pertain more to abilities in reading/read comprehension (Mangina, 1981, 1994a,b,c, 1998). More specifically, the Mangina-Test stimuli were constructed to have a particular meaning as described below:

1) Direction: implies the exact discrimination of same stimuli differing only in left–right angular position within the same axis and inserted (masked) within a complex configuration of stimuli.
2) Spatial orientation: implies the exact discrimination of same stimuli differing only in rotation upwards or downwards, or rotation sidewards 45°–90° and inserted (masked) within a complex configuration of stimuli.

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3) Size: implies the exact discrimination of same stimuli differing only in size (volume) and inserted (masked) within a complex configuration of stimuli.

4) Dimension: implies the exact discrimination of similar (same looking) stimuli with alterations in breath and/or length and inserted (masked) within a complex configuration of stimuli.

5) Mixed: (direction, spatial orientation, size, dimension): implies the exact discrimination of all of the above parameters combined when they coexist within a complex configuration of stimuli.

Most importantly, 16 of the 44 stimuli pairs pertaining to the perceptual analysis of size and dimension have been found to be related more to mathematical abilities (MATH). Another 16 stimuli pairs pertaining to direction and spatial orientation were found to be related more to abilities in reading and reading comprehension (READ). The remaining six stimuli pairs pertain to combined geometrical properties as they relate to both reading comprehension and mathematical abilities (MIXED) (for more details, including data pertaining to the standardization, validity, scoring and interpretation of the Mangina-Test, see Mangina, 1981, 1994a,b,c, 1998).

“Analytical-specific visual perception” as measured by the Mangina-Test is a more complex process than simple sensory perception itself. In this context, “analytical-specific visual perception” is the ability of cerebral structures to discriminate (identify) simple stimuli inserted (masked) in other increasingly more complex stimuli, according to their exact direction, spatial orientation, size, dimension and shape within a limited span of time (for details of this testing procedure including data pertaining to the standardization, validity, scoring and interpretation of the Mangina-Test, see Mangina, 1981, 1994a,b,c, 1998). Children, adolescents and adults with varying degrees of learning abilities or disabilities may not generally experience difficulty with sensory perception since it involves simple discrimination of stimuli. However, they do experience varying degrees of difficulties with “analytical-specific perceptual skills”, which involve a more complex thinking process in cognizing analytically very subtle perceptual relationships of exact similarities and differences within a limited span of time (Mangina, 1998).

It has been shown that the inferior parietal cortex has been consistently involved, along with the contribution of the lateral prefrontal and premotor cortices, in calculation and mathematical problem-solving tasks through their role in retrieval and mental representation (Dehaene et al., 1999; Gruber et al., 2001; Zago et al., 2001). On the other hand, several studies reliably confirmed that reading and verbal abilities involve the temporo-occipital visual representation (Dehaene et al., 1999; Guenther, 2003; Jobard et al., 2003; Flowers et al., 2004; Schlaggar and McCandliss, 2007; Casarotto et al., 2008). Therefore, common activations across mathematical and reading tasks cover a distributed cortical network comprising mostly left-sided prefrontal, premotor and parietal areas related to visuo-spatial, linguistic, attentional and mnemonic processes.

In our previous functional study (Mangina et al., 2008a, 2009-this issue), we determined the neural correlates of analytical-specific visual perceptual processes as measured by the Mangina-Test. Our findings supported the existence of a distributed functional neural network that links prefrontal cortex to occipito-temporal and parietal regions, and its activity correlated with the level of task difficulty, and thus, with the attentional and visual analytical perceptual processing resources needed.

In this second study of the same functional dataset, we aimed at assessing as to how neural activity may be differentially modulated by the category-specific perceptual relationships of the Mangina-Test. Therefore, this investigation was carried out to verify the following points: a) the brain correlates of the behavioral association between the specific perceptual analysis of the size and dimension stimuli pertaining to abilities in mathematics as opposed to b) the perceptual analysis of stimuli dealing with direction and spatial orientation which pertain more to abilities in reading comprehension, and c) to both of the above parameters.

2. Methods

2.1. Participants

Twelve right-handed young (mean age 26±3 years; 6 females) healthy adult volunteers were enrolled in the study. All participants were normotensive, had no abnormalities on routine blood and urine tests, brain MRI, and no history of relevant medical, neurological or psychiatric disorders. All were medication-free for four weeks prior to the study, including over the counter medications.

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 task and image acquisition

The visual stimuli of the fMRI session reproduced 44 simple and 44 complex original geometrical stimuli of the Mangina Diagnostic Tool of Visual Perception (Mangina-Test). The Demonstration section and the first four pairs of stimuli of the Mangina-Test were used to familiarize participants with the task. The 5th-to-44th stimuli were presented in a pseudo-randomized order during the fMRI session, as described in Mangina et al. (2009-this issue). The task of the Mangina-Test consists of identifying a simple stimulus which is masked (inserted) into a simultaneously presented complex configuration, according to subtle geometrical relationships.

The Mangina-Test was administered according to the steps described in the Manual for the Mangina Diagnostic Tool of Visual Perception (Mangina, 1998). Pictures were presented on a rear projection screen viewed through a mirror (visual field: 25° wide and 20° high). Stimulus presentation and subjects’ responses were handled by using the software package Presentation (http://www.neurobehaviorsystems.com). Each fMRI run contained eight stimuli pairs and lasted 270 s, including 15 second rest at the beginning and at the end of a stimulation block. Participants were instructed to carefully look at 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 when pressing the response button. Therefore, stimulus duration was self-paced and corresponded exactly to the response time for identifying the simple stimulus within the complex one.

2.4. Image acquisition

Multi-slice axial echo-planar images (EPIs) were acquired on a 1.5 Tesla MRI scanner (GE Medical Systems Signa) with TE = 40 ms, TR = 2.5 s, flip angle 90, FOV = 240 mm with 64 x 64 acquisition matrix (3.75 mm x 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 the 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 T1-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).

A paper-and-pencil version of the Mangina-Test was administered immediately after scanning, in order to counter-check the correct responses given during the fMRI session and to verify analytical-specific perceptual skills.

2.5. Behavioral analysis

Accuracy and response time (RT) were measured for MATH, READ, and MIXED stimuli during scanning. For accuracy data, a no response within the 30 second presentation of the stimuli was considered as an error and deleted from the analysis. Similarly, when an incorrect response was given in the post-scan paper-and-pencil administration of the test, a no response was considered for that item in the within stimulus category group-averaged RT or accuracy. For RT, individual averages within stimulus category were analyzed. Subjects’ performances were analyzed using repeated measures analysis of variance (ANOVA) for RT, and non-parametric Friedman’s test for accuracy by using Stat-View 5.0.

2.6. Image analysis

We used the AFNI package to analyze functional imaging data (http://afni.nimh.nih.gov/afni, Cox, 1996). All volumes from the different runs were concatenated and coregistered (3dvolreg program), temporally aligned (3dTshift), spatially smoothed, and normalized to the percent signal change as described in Mangina et al. (2009-this issue). The brain activity for each single stimulus was modeled with a separate regressor obtained by convolving a standard hemodynamic response model with a square wave of duration corresponding to the response time of the stimulus itself. The six movement parameters derived from the motion correction were included as regressors of no interest. As specified elsewhere (Mangina et al., 2009-this issue), the area subtended to single-item BOLD response was considered as an index of brain activation. The significance of the response to each type of stimulus according to their geometrical properties was calculated using a general linear test that aggregated data across all regressors for the correlated ability — size and dimension for mathematical abilities, direction and spatial orientation for reading and reading comprehension, combined features for mixed stimuli.

Individual unthreshed responses for each of the stimuli of interest were transformed into the Talairach and Tournoux Atlas coordinate system (Talairach and Tournoux, 1988), and resampled into 1 mm³ voxels for group analyses. Mixed-effect model analysis of variance (one-way within-subjects ANOVA) — with 12 subjects as random factor and stimulus category as fixed factor (3 levels: MATH, READ, and MIXED stimuli pairs) was applied by using the unthresholded responses to different stimulus types to construct T contrasts and identify the patterns of neural response to different stimulus types, or significant differences across conditions (e.g. MATH vs. READ, or [MATH+READ] vs. MIXED). For the patterns of activation associated with different stimulus types (corresponding to a one-sample T-test), statistical significance was established at a voxel-level p value < 0.01, False Discovery Rate corrected. For all stimulus types × subjects interactions, statistical significance was established at an uncorrected voxel-level p value < 0.05, and required a minimum cluster volume of 100 µL, cluster connection radius 1.01 mm. Activations were anatomically localized on the group-averaged Talairach transformed T1-weighted images.

Volume means were extracted from significant clusters of the T contrasts for the comparison among stimulus types, and plots of parameter estimates in selected regions of interest showed across subjects-averaged BOLD responses (percent change) for MATH, READ and MIXED stimuli.

3. Results

3.1. Behavioral results

All subjects were able to accomplish adequately the task. Performance was not significantly different among stimulus categories (MATH, READ and MIXED) across subjects, neither for accuracy nor for reaction times (accuracy: Friedman’s test X² = 5.1; RT: F(2,22) = 1.09; p = n.s.).

Fig. 1. Statistical maps showing brain regions activated during the visual presentation of different stimuli (MATH, READ, and MIXED) of the Mangina-Test as compared to rest baseline (FDR corrected p < 0.01). Spatially normalized activations are projected onto a single-subject left hemisphere template of an inflated brain in the Talairach space. Ventral occipito-temporal (V-OT) and dorsal occipito-parietal (D-OP) extrastriate areas, intraparietal (IPS) and sensorimotor cortex (SM), superior (SPL) and inferior parietal (IPL) lobules, temporoparietal junction (TPJ), middle and superior temporal (MT/ST), posterior cingulate (PC), supplementary motor area (SMA), frontal eye field (FEF), ventral premotor (vPM), inferior frontal (IF), medial frontal (MedF) cortex, nucleus caudatus (NC) and thalamus (THA).
3.2. fMRI results

3.2.1. Neural patterns of brain activation during the visual presentation of different stimuli of the Mangina-Test as compared to rest baseline

A common functional network of brain areas was activated by the presentation of MATH, READ or MIXED stimuli of the Mangina-Test (voxel-level $p$ value $<0.01$, FDR corrected). Specifically, overlapping task-related activations across different stimuli types were found bilaterally in the ventral occipito-temporal (V-OT) and dorsal occipito-parietal (D-OP) extrastriate areas, intraparietal sulcus (IPS) and sensorimotor cortex (SM), superior (SPL) and inferior parietal (IPL) lobules, supplementary motor area (SMA), frontal eye field (FEF), ventral premotor (vPM), insula/inferior frontal (IF), dorsolateral prefrontal cortex (DLPFC), and basal ganglia (Fig. 1). Distinctively,
posterior parietal regions (such as IPS and SPL), vPm, DLPFC, anterior cingulate (AC) and thalamus (THA) appeared to be recruited to a larger extent for MATH stimuli, whereas medial occipito-temporal cortex was predominantly activated by READ stimuli (Fig. 1). Cortical regions involved in the default mode system (Raichle and Snyder, 2007) showed significantly reduced activation as compared to rest condition, e.g. bilateral precuneus and posterior cingulate (PC), medial prefrontal cortex (MedPF), middle temporal cortex and temporo-parietal junction (TPJ) (Fig. 1).

3.2.2. Stimuli related to mathematical abilities (size and dimension) vs. stimuli associated with abilities in reading comprehension (direction and spatial orientation)

The direct comparison between MATH and READ stimuli showed significant differences in the magnitude and extent of activation in brain regions related to the performance of the Mangina-Test (Figs. 1 and 2). Higher activation for the MATH stimuli was found in a bilateral fronto-parietal network including, DLPFC, vPM, FEF, IPL, AC and dorsal occipital extrastriate areas. Additional MATH-related activations were found in the THA and in the ventrotemporal extrastriate cortex (i.e. fusiform gyrus). In contrast, READ stimuli showed a stronger recruitment in bilateral sensorimotor areas, medial occipital extrastriate cortex (i.e. lingual gyrus), amygdala/parahippocampal, and right inferior frontal cortex. Moreover, a smaller deactivation of some cortical regions involved in the default mode network, such as the TPJ and middle temporal cortex, was associated to READ as compared to MATH stimuli (Table 1).

Volume means obtained from significant clusters identified in the stimulus type comparisons illustrate significant higher response to MATH stimuli (e.g. dorsal occipital and DLPFC), or READ stimuli-associated higher activations (e.g. bilateral sensorimotor areas and medial occipital extrastriate cortex). As expected, cortical regions involved in the default mode network that showed significant differences for different stimulus types (e.g. TPJ) showed a smaller deactivation for READ as compared to MATH pairs (Fig. 2).

3.2.3. Specific activations associated with stimuli pertaining to mixed abilities

A weighted comparison was used to identify specific neural responses to different stimulus categories (MATH and READ vs. MIXED stimuli). As compared to MIXED pairs, MATH and READ stimuli showed a significantly higher recruitment of a premotor, posterior parietal and ventral occipito-temporal network of brain regions that were commonly active during the execution of the Mangina-Test (Mangina et al., 2009-this issue). Furthermore, brain regions of the default mode network showed a higher deactivation as compared to MIXED pairs (Fig. 3). In contrast, MIXED stimuli showed a significantly higher activity bilaterally in posterior parahippocampal regions as compared to MATH and READ stimuli together (Fig. 3).

4. Discussion

In a previous functional MRI study (Mangina et al., 2009-this issue), we determined the neural correlates of analytical-specific visual perceptual processes as measured by the Mangina-Test. Our findings supported the existence of a distributed functional neural network that links prefrontal cortex to occipito-temporal and parietal regions, and its activity correlated with the level of task difficulty and thus, with the attentional and visual analytical perceptual processing resources needed. As detailed in our original work, the fronto-parietal and extrastriate regions activated during the performance of the Mangina-Test, have been extensively related to object recognition, spatial processing, visual search and attention orienting (Haxby et al., 1991; Culham et al., 1998; Marshall and Fink, 2001; Corbetta et al., 2008). Within this distributed neuronal network, activated during the administration of the Mangina-Test, analytical-specific perceptual processes for MATH, READ and MIXED stimuli rely on partially distinct brain circuits. A common functional network of brain areas, involving the bilateral prefrontal–premotor–parietal network and both ventral and dorsal extrastriate areas, was activated by the presentation of MATH, READ or MIXED stimuli, thus, overlapping with the originally described neural correlates of analytical-specific visual perceptual processes. Typically, bilateral posterior parietal, premotor and prefrontal regions along with the anterior cingulate, appeared to be recruited to a larger extent for MATH stimuli. On the other hand, READ stimuli predominantly activated bilateral medial occipito-temporal, amygdala/parahippocampal and sensorimotor cortices and the right inferior frontal cortex. Moreover, the posterior parahippocampal cortex showed a higher activity for MIXED stimuli.

Altogether, these findings demonstrate that the exact discrimination of very subtle geometrical relationships distinctly modulates cerebral activity, so that category-specific brain responses can be

<table>
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a For each significant cluster, coordinates of the local maxima, estimated Brodmann’s areas from Talairach and Tournoux atlas (Talairach and Tournoux, 1988), and T-values of significance are provided.

b Statistical significance for MATH vs. READ interaction was assumed at p<0.05 uncorrected, and required a minimum cluster volumes of 100 μL. Interactions where MATH stimuli showed higher BOLD increases than READ stimuli are reported with a positive T-value, while brain areas responding more to READ stimuli are reported with a negative T-value.

c x = distance in millimeters to the right (+) or the left (−) side of the midline.
y = distance anterior (+) or posterior (−) to the anterior commissure z = distance superior (+) or inferior (−) to a horizontal plane through the anterior and posterior commissures.
related to identifiable cognitive abilities. Consistent with previous studies on number/math processing (Dehaene et al., 1999; Gruber et al., 2001; Zago et al., 2001), parietal, premotor and prefrontal regions’ activity appears to be more related to MATH stimuli, while READ-associated activations found in the medial occipito-temporal cortex, motor-related areas and inferior frontal region are consistent with previous findings in functional imaging studies of reading/reading comprehension (Price, 2000; Guenther, 2003; Jobard et al., 2003; Flowers et al., 2004; Schlaggar and McCandliss, 2007; Casarotto et al., 2008).

Previous research conducted with the direct electrical stimulation of specific human brain structures applied through intracerebral...
electrodes with the concomitant recording of bilateral electrodensal activity revealed that limbic structures such as the amygdala, the anterior and posterior hippocampi and the anterior cingulate gyri are potent ipsilateral moderators of bilateral electrodensal activity as opposed to neocortical sites (Mangina and Beuzeron-Mangina, 1994, 1996). Bilateral electrodensal activity was chosen as a convenient autonomic indicator to activate limbic structures that are important for learning and memory functions. Manipulations of standardized bilateral electrodensal activity coupled with stimulation using analytical-specific visual perceptual tasks derived from the Mangina-Test, has been applied within a psychophysiological treatment methodology for learning disabilities and the improvement of learning abilities (Mangina, 1986, 1989, 1991, 1993; Mangina and Beuzeron-Mangina, 1988, 1992a, b, 2004a, b; Mangina and Sokolov, 2006). Interestingly, in our present investigation, the amygdala and anterior parahippocampal cortex show a stronger recruitment during the presentation of READ stimuli. Moreover, MIXED stimuli additionally recruited the posterior part of the parahippocampal cortex. Thus, these data strongly support the fundamental role of these limbic structures and cortico-limbic connections in modulating central and peripheral responses to complex cognitive operations, such as analytical-specific perception used in the psychophysiological treatment procedure for the treatment of learning disabilities and the improvement of learning abilities (Mangina and Beuzeron-Mangina, 1996, 2004a, b).

Based on empirical research and clinical applications, learning ability has been defined as the psychophysiological condition consisting of a multiplicity of cerebral cortico-limbic neuronal synaptic and dendritic interconnections coupled with "optimally high" physiological activation which result in increasing degrees of "analytical-specific perceptual skills" necessary for selective and sustained information processing and the acquisition of new and complex tasks (Mangina, 1998; Mangina and Beuzeron-Mangina, 1992a, b, 2004a, b; Mangina et al., 2000; Mangina and Sokolov, 2006). The findings of the present investigation with additional analysis of our brain functional imaging data on the neural correlates of the Mangina-Test (Mangina et al., 2008a, b, 2009-this issue) contribute to the elucidation and understanding of the psychophysiological and neurobiological bases of analytical-specific perceptual skills, and their fundamental role in the development of learning abilities.

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