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A Functional Magnetic Resonance Imaging Study of the Cognitive Estimation

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Abstract

The Cognitive Estimation Test (CET) represents a novel diagnostic tool for quantifying the ability to provide accurate cognitive estimates. Cognitive estimates are supposed to result from frontal cortex activity. The general aim of our study was to evaluate the brain regions responsible for cognitive estimation. In a group of ten healthy volunteers we used functional magnetic resonance imaging (fMRI) to detect the brain systems involved in cognitive estimation. Four blocks of experimental estimation condition alternated with the control condition with each block consisting of 8 visually-presented questions.

We have confirmed that the CET increases the fMRI signal in the left inferior frontal gyrus (Brodmann's Area, BA 47) and the left middle frontal gyrus (BA 9). Further we detected activation in the bilateral lingual gyrus (BA 18), right superior parietal lobule (BA 7) and cerebellum. These data indicate that CET is connected not only with frontal but also with parieto-occipital system activation.

Introduction

The Cognitive Estimation Test (CET) represents a relatively simple task that can be administered under different clinical situations. This test was originally designed to examine the estimating abilities (Shallice & Evans 1978). Authors of CET were the first investigators to draw attention to a particular cognitive deficit, namely the 'gross inability to produce adequate cognitive estimates'. Cognitive Estimation Test was developed to quantify the ability to provide accurate cognitive estimates in patients with frontal lobe damage (Shallice & Evans 1978). Patients were asked to answer certain questions with unknown but approximately estimable answers such as 'What is the length of an average man's spine?' or 'How fast do race horses gallop?'. The authors later confirmed that patients with anterior lesions performed the CET significantly worse than patients with posterior lesions, and this did not seem to be a consequence of deficits in general intelligence.

Even thought the Cognitive Estimation Test was proved with respect to frontal damage lesions (Kopelman 1991; Mendez *et al* 1998; Shoqeirat & Mayes 1991; Taylor & O'Carroll 1995), no functional neuroimaging study focusing on CET has yet to be published. Moreover, some studies (Duncan *et al* 1995; Taylor & O'Carroll, 1995) present doubts on the localizing ability of the CET and insensitivity to frontal or other dysfunction.

The neuroanatomical basis of the cognitive processes involved in estimation tasks are likely to be spread widely throughout the cortex and a functional neuroimaging study would be the next step in furthering our understanding of the functional neuroanatomy of these processes.

The general aim of our study was to evaluate the brain regions responsible for cognitive estimation by the use of functional magnetic resonance imaging (fMRI). In a group of 10 healthy volunteers, we used functional magnetic resonance imaging to detect the brain systems activated by cognitive estimation.

Methods

Sample

Ten right-handed healthy volunteers recruited via a local advertisement participated in the experiment after giving written informed consent. The main exclusion criteria for control subjects were a personal history of any psychiatric disorder or substance abuse established by the Structured Clinical Interview for DSM-IV. The local Ethics committee approved the fMRI study.

Experimental task (CET) and fMRI acquisition

Under the experimental conditions, subjects were instructed to answer questions presented visually by the use of an LCD projector placed outside the scanner. The estimation blocks for the cognitive estimation consisted of 11 original CET tasks from the Czech validated form of the test (Preiss & Laing 2001). Due to the experimental design, additional questions were added to form a total number of 32 questions. The additional questions were constructed by one of the authors of the Czech version of the CET (M.P.). The selection of additional questions for cognitive estimation was based on pre-exploration during the process of validation of the Czech CET (Preiss & Laing 2001). These additional questions were slight modifications of the original questions. For example the CET question 'What is the length of a tennis court?' was modified to obtain the additional question, 'What is the length of a football field?'.

The non-estimation blocks, for comparison with the estimation, consisted of simple questions not requiring any estimating as they had well-known answers (for example: 'How much is two and two tennis courts?'). The questions for these blocks were selected according these criteria: (1) the content of the non-estimation questions referred to the similar qualities as in the active estimation, for example the active question 'What is the weight of a full bottle of beer?' was paired with the control question 'How much is three bottles minus two bottles?' (2), the non-estimation questions had very evident answers which needed only reading, sentence comprehension and simple exact calculation (addition and subtraction up to five). Reading, comprehension and some simple calculation were also involved in estimation blocks. Hence, using these criteria for baseline (non-estimation) blocks, the cognitive process of straight estimation is the major difference between both conditions during fMRI.

Sixty four T2*-weighted volume images were acquired during each measurement on a 1.5-T Siemens Magnetom Vision (Siemens, Erlangen Germany) using a single-shot gradient echo EPI sequence (TR=7 s, TE=54 ms, flip angle=90°) in 27 oblique slices of 4 mm thickness each. The matrix size was 128 x 128, with a voxel size of 1.8 × 1.8 × 4 mm. Head movement was minimized by a forehead strap. Each condition was presented in blocks lasting 56 s, with eight presentations of given questions per block and an interstimulus interval of 7 s. The experimental estimation condition alternated with the control condition, and four blocks of each condition were performed.

To avoid the motion artifacts made by verbal response, the subjects were instructed to read and answer the estimation and control questions during the fMRI scanning without vocalization, immediately after the fMRI investigation, at which time the answers were registered.

fMRI data analysis and statistics

The data analysis was performed using SPM99 (http://www.fil.ion.ucl.ac.uk/spm) implemented in Matlab (Mathworks, USA). As a pre-processing step, the EPI images were realigned to the first one and all volumes were resliced with sinc interpolation. Normalizing an individual T2 image to the MNI-ICBM template was performed in two steps: (1) estimating the normalizing parameters and (2) writing the normalized images using these parameters. All volumes were smoothed with a full width at half maximum of 6 mm isotropic Gaussian kernel. Statistical analyses were performed for all individual subjects in the 1st level analysis and in the 2nd level (group) analysis for a population inference. In the 1st level analysis the hemodynamic response was modeled with a boxcar function convolved with a haemodynamic response function with a delay of 6 s. Confounds of global signal changes were removed by applying a high pass filter (cut-off cycle was 128 s). Next, the estimated means of each condition were compared with a *t*-test in every voxel independently. After transformation of *t*-values to *Z*-values, statistical parametric maps of *Z*-values were created and the anatomical locations of the activated areas were determined in the normalized space. To evaluate the group effect of CET activation, the contrasts from individual evaluations were analyzed by the one sample t-test. This method tests the null hypothesis that the mean of one group of observations is identical to zero. The p-values ≤ 0.001 uncorrected for multiple comparisons at a single voxel level at each cluster level were used with a minimum of 20 voxels over the threshold. For rigorous control type I error we accepted as significant only conservative family-wise error (FWE) corrected findings ($p \leq 0.05$) for the cluster level statistic.

Analyzing the neuropsychological data, the standardized versions of the CET weighted scores were calculated for further analyses. The weighted scores were derived from the mean and standard deviation of the standardized sample (Preiss & Laing 2001; Preiss *et al* 2003), where no point was given for the performance up to 1 standard deviation (SD) above or below the mean, one point for the performance from 1–2 SD above or below the mean and two points 2 and more SD above or below the mean. To compare demographical variables, two tailed t tests and chi-square were used.

Results

Behavioral and demographic data

A separate group of 10 healthy, right-handed volunteers, 7 women and 3 men, average age 24.8 yrs (21–33 yrs, SD=4.0), average education 7.1 (SD=2.7) on the scale 0–11 where 7 is between 12–14 yrs of education (higher than secondary and lower than bachelor degrees). Laterality score was 10.2 (SD=1.4) according to Annett (Annett 1972).

All the non-estimation (baseline) questions were answered correctly in all subjects. The CET score of 4.6 (SD=1.8) measured after imaging is within the Czech norm (Preiss & Laing 2001). There were no differences between men and women in age (F=4.59, df=8, p=0.301), CET score (F=2.30, df=8, p=0.251), education (Chi-square=7.61, df=5, p=0.178) or laterality (F=1.08, df=8, p=0.856).

fMRI Data

The Cognitive Estimation Task relative to the non-estimation condition increased the BOLD (blood oxygen-level-dependent) signal in the left lingual gyrus Brodmann's Area (BA) 18, the right lingual gyrus (BA 18), the left Inferior frontal gyrus (BA 47), the left middle frontal gyrus (BA 9), the right superior parietal lobule (BA 7), the left medial frontal gyrus (BA 8), and the right white cerebellar matter (Table 1, Figure l).

The Cognitive Estimation Task relative to the non-estimation condition had decreased the BOLD signal in the right caudate head, the left medial frontal gyrus (BA 10), the right precentral gyrus (BA 6), the right anterior cingulate (BA 32), and the left mediofrontal white matter (Table 1, Figure 2).

The number of voxels exceeding the height (T=4.14 for p=0.001) and extent of the threshold (k=20 voxels) was lower for the contrast indicating decreased BOLD signal (deactivation) by the CET (N=160) than for the contrast indicating activation (N=780).

Discussion

In our experiment we have demonstrated that the Cognitive Estimation Test influences brain activity in the frontal, parietal and occipital brain regions. The increase of the BOLD signal in the left middle and inferior frontal gyrus (BA 9 and 47) supports the hypothesis that the outcome of the CET reflects prefrontal cortex activity in the dominant hemisphere. This postulate was previously formulated only on the basis of clinical observations in patients with frontal lesions (Kopelman 1991; Mendez *et al* 1998; O'Carroll *et al* 1994; Shoqeirat *et al* 1990; Taylor & O'Carroll 1995).

The activation in both areas of the frontal cortex in the CET embodies some similarities to the contrasts obtained from functional neuroimaging studies focused on other cognitive domains. The activation of middle frontal gyrus (BA 9) in the dominant hemisphere has been observed in sustained attention tests (Coull & Nobre 1998) and in mental imagination of static (Kosslyn *et al* 1996) and rotation objects (Kosslyn *et al* 1998). As the BA 9 is close to the supplementary motor cortex and Broca's region, this area is commonly activated also in verbal tasks (Binder 1997). The middle frontal gyrus was identified as being activated in numeric, object and spatial working memory tests (Coull *et al* 1996; de Zubicaray *et al* 1998; Owen *et al* 1996a; Petrides *et al* 1993), in problem solving tasks as the London Tower Test and the Wisconsin Card Sorting Test (Goldberg *et al* 1998; Owen *et al* 1996a), in semantic memory retrieval (Klein *et al* 1995; Martin *et al* 1995; Wise *et al* 1991) and epi-

Tab. 1. The regional brain activity changes associated with the Cognitive Estimation Test relative to the passive (non-estimation) condition for clusters consisting of ≥20 voxels and exceeding height threshold T=4.14 (p≤0.001). Marked (*) are the clusters with p≤0.05 after FWE correction across the whole brain.

Cerebral region	Hemisphere	k_E	X	y	z
Activation by CET					
Lingual Gyrus (BA 18)	L	166*	–14	–78	–12
Lingual Gyrus (BA 18)	R	149*	16	–74	–12
Inferior Frontal Gyrus (BA 47)	L	79 *	–52	32	–8
Middle Frontal Gyrus (BA 9)	L	142*	–58	22	30
Middle Frontal Gyrus (BA 9)	L	26	–36	20	28
Lingual Gvrus (BA IS)	L	105 *	–12	–54	6
Superior Parietal Lobule (BA 7)	R	36	38	–68	52
White matter Cerebella	R	23	36	–50	–42
Medial Frontal Gvrus (BA 8)	L	32	–12	28	38
White matter Cerebella	R	22	22	–62	–20
Deactivation by CET					
Caudate Head	R	45	6	22	4
Medial Frontal Gvrus (BA 10)	L	24	–10	52	–12
Precentral Gyrus (BA 6)	R	27	48	–8	22
Anterior Cinsulate (BA 32)	R	21	8	34	–12
Mediofrontal white matter	L	43	–12	30	2

Note: R, right; L, left; BA, Brodmann's Area; x, y, z coordinates of the Talairach space for each maximum; k_E, is the number of voxels extended the threshold of 20 or more.

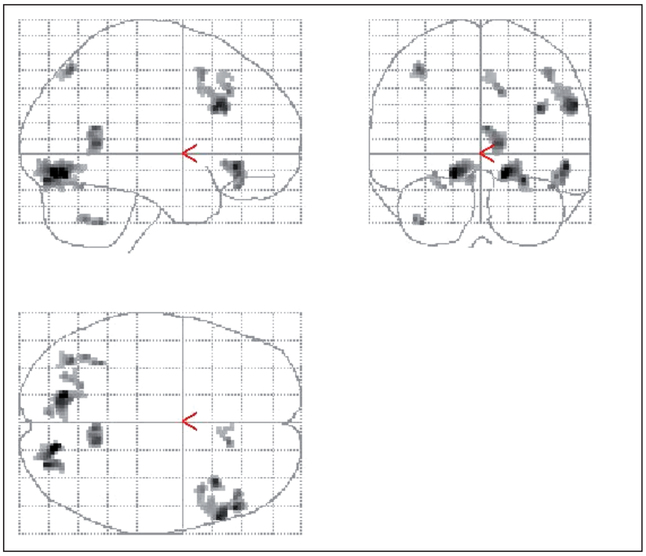

Fig. 1. The areas of activation (increase of BOLD signal) associated with the Cognitive Estimation Test relative to the baseline condition. Significant results ($p \leq 0.001$, cluster ≥20 voxels) are displayed. Talairach coordinates and number of voxels in each cluster is presented in Table 1.

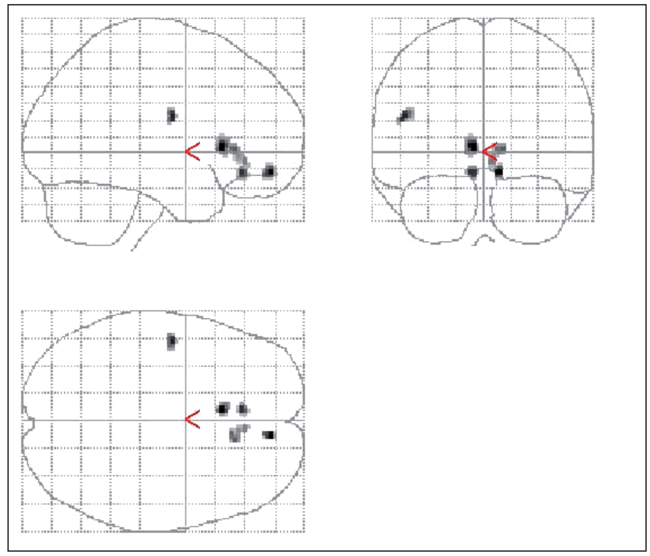

Fig. 2. The areas of deactivation (decrease of BOLD signal) associated with the Cognitive Estimation Test relative to the baseline condition. Significant results ($p \leq 0.001$, cluster ≥20 voxels) are displayed. Talairach coordinates and number of voxels in each cluster is presented in Table 1.

sodic memory encoding (Kelley *et al* 1998; Wagner *et al* 1998). It is notable that in episodic memory retrieval, the activation of BA 9 is rarely observed.

The second frontal area activated in our study by the cognitive estimations is the inferior frontal gyrus (BA 47). This gyrus is involved in language processing (review in Cabeza & Nyberg 2000), spatial working memory (Owen *et al* 1996a; 1998), problem solving (Berman *et al* 1995; Goel *et al* 1997; Goldberg *et al* 1998), semantic memory (Demb *et al* 1995; Kapur *et al* 1994; Vandenberghe *et al* 1996; Martin *et al* 1995), and in the encoding of episodic memory (Owen *et al* 1998; Wagner *et al* 1998).

All these functions of inferior and middle frontal gyrus would be involved in the cognitive process underlying the cognitive estimation. With the respect to the cognitive estimation it is notable that in episodic memory retrieval, the activation of both frontal gyruses is only rarely observed (Andreasen *et al* 1995a, 1995b) and so it is less probable that narrative imagination underlies the CET.

The third region with a significant increase in the identified BOLD signal is the lingual gyrus (BA 18), the area below the calcarine sulcus functionally close to the V2 region of the visual cortex. The higher bilateral activation of the lingual gyrus has been found in attention (Coull *et al* 1996; Coull & Nobre 1998; Pardo *et al* 1990; Pardo *et al* 1991) and other cognitive tests presented visually (Goldberg *et al* 1998; Kosslyn *et al* 1996; Kosslyn *et al* 1998; Owen *et al* 1996a, 1996b; Petrides *et al* 1993). Due to the visual presentation of CET during our fMRI experiment, the increase in the BOLD signal in the experimental estimation condition compared to the control condition could reflect an increase of attention during blocks of active estimates or the more specific cognitive processes.

The interpretation of other areas activated in the CET as well as deactivated regions would be approached with caution due to their lower statistical significance after correction for multiple analyses. The decrease in the BOLD signal in the mediofrontal cortex (BA 10) and anterior cingulate (BA 32) would imply that the typical cognitive activation of these regions, such as the rapid response selection characteristic of the Stroop test (Bench *et al* 1993; George *et al* 1997; Pardo *et al* 1990), is not involved in the process of cognitive estimation. It is possible to expect that a different type of conflict solving paradigm would be necessary for adequate cognitive estimation. The regions of deactivation would also represent the part of a nonspecific baseline default mode (Raichle *et al* 2001) suspended during cognitive estimation.

However, it is difficult to separate the particular cognitive functions from each other and heuristic analysis based on comparison of typical neuroimaging patterns of different cognitive functions would not be plausible. A useful conceptual framework for the interpretation of our findings is an analogy of dissociable systems theory in terms of mathematical thinking. This concept supposes two different neuronal systems are necessary for exact and approximate calculation (Dehaene & Akhavein 1995; Dehaene *et al* 2004). The exact calculation represents the language-based format ability to process and store arithmetic operations and knowledge (such as multiplications). The approximate calculation is preverbal and language independent and occurs by manipulation with quantity manipulation and approximation (such as first glance comparison of two groups of dots). Exact calculation tasks revealed strictly left-lateralized activation in the inferior frontal lobe, cingulated cortex, and precuneus, right parieto-occipital sulcus, bilateral angular gyri, and middle temporal gyrus. Approximate calculation activates bilateral parietal lobes (intraparietal sulci, postcentral gyrus, and inferior parietal lobule), right precuneus, bilateral precentral sulci, left dorsolateral prefrontal cortex and left superior prefrontal gyrus (Dehaene *et al* 1999). The exact arithmetic knowledge and skills are acquired during training with exact problems, and are stored in a language-specific format which require the activation of language areas. Approximate arithmetic, in contrast, shows item and language independence and relies primarily on a quantity representation implemented principally in the parietal lobes. Our findings of Cognitive Estimation Test fMRI activation in the parietal and occipital cortex, left inferior and middle frontal gyrus support the similarities with approximate calculus processing.

It is interesting that the same areas are also involved in the tasks of mental rotations (Kawamichi *et al* 1998; Kosslyn *et al* 1998), visually guided movements (Kawashima *et al* 1996), and attention orienting (Corbetta *et al* 1993). The neurobiological substrate for both the CET and approximate arithmetic would rely on a dorsal parieto-occipital pathway involved in the approximate representation of numerical quantities and visuo-spatial processing and imagination. In contrast, the control, non-estimation conditions were connected with the increase of the BOLD signal mostly in the mediofrontal and cingulated cortex. These areas are among others involved in the exact calculations, and the finding confirms that in the control condition the simple exact arithmetic operations were done (for example 'How much is three bottles minus two bottles?').

In conclusion, the estimation process is connected with the activation of middle dorsal and inferior dorsal frontal cortex and dorsal parieto-occipital system. The frontal areas of the dominant hemisphere supply the attention, language processing and semantic memory retrieval of the virtual CET situations. Because the solutions of the tasks implied in the CET are not well known, episodic memory retrieval is not active and the static and dynamic mental imageries offer the implements for the processing of the CET. The particular steps of problem solving connected with the estimations are monitored by working memory and the solutions are finally encoded in episodic memory. The strategy in selecting the best possible response (and inhibition of the others) is different than in the Stroop test-like paradigm and this aspect explains the absence (or decrease) of activation in the anterior cingulate. The core process to select the best answer is performed in the dorsal parieto-occipital system. The cognitive estimation depends on approximate representation, manipulation and approximation of numerical quantities and visuo-spatial processing and imagination (as in mental rotations).

These proposed models of the cognitive processes involved in estimations that are based on functional neuroimaging only partially conform to the early models from a clinical basis (Shallice & Evans 1978; Freeman *et al* 1995). The Cognitive Estimation Test seems to be a unique and complex task reflecting the corresponding function of frontal cortex and parieto-occipital system. The CET would be sensitive not only for patients with frontal damages but also for patients with parietal subtype of acalculia. These patients with parietal lesions exhibit the loss of the sense of numerical quantity (approximations) with relatively preserved language-based exact arithmetic (Lemer *et al* 2003). This hypothesis needs further experimental verification on specific populations.

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