ISSN 0362-1197, Human Physiology, 2015, Vol. 41, No. 6, pp. 611–624. © Pleiades Publishing, Inc., 2015.
Original Russian Text © S.V. Kuptsova, M.V. Ivanova, A.G. Petrushevsky, O.N. Fedina, L.A. Zhavoronkova, 2015, published in Fiziologiya Cheloveka, 2015, Vol. 41, No. 6, pp. 49–64.

Sex-Related Differences in Task Switching: An fMRI Study

S. V. Kuptsova[a, b], M. V. Ivanova[c], A. G. Petrushevsky[a], O. N. Fedina[a], and L. A. Zhavoronkova[b]

[a] *Center for Speech Pathology and Neurorehabilitation, Moscow, Russia*

[b] *Institute of Higher Nervous Activity and Neurophysiology, Russian Academy of Sciences, Moscow, Russia*

[c] *National Reseach University Higher School of Economics, Moscow, Russia*

e-mail: svoky@rambler.ru

Received September 30, 2014

Abstract—Executive functions are the important human ability to program, regulate, and control the implementation of various cognitive processes, such as voluntary task switching. However, sex-related features of this process have not been characterized in sufficient detail. These distinctive features were studied using functional magnetic resonance imaging (fMRI) and neuropsychological examination. Seventy healthy subjects 21–48 years of age (36 men and 34 women) were involved in the study. During an fMRI experiment, the subjects had to shift their attention between two tasks (classifying figures according to their form or number). In neuropsychological examination participants completed a series of visual attention, task switching, and memory tests. The fMRI study revealed that a neuronal network controlling task switching in women includes the dorsolateral prefrontal and inferior parietal cortical areas, as well as the secondary areas of the visual cortex in the left hemisphere (LH) and the right hemisphere (RH), and cortical areas of the left and right hemispheres of the cerebellum. The same areas were activated in men and additional sites of activation were detected in the supplementary motor area, right insula, and left thalamus. Comparison of the groups of men and women revealed significantly stronger activation of the prefrontal areas in both LH and RH, the left parietal lobe, and the right insula in men, and moreover activation of the supplementary motor area was observed in men but not in women. Neuropsychological testing showed that men took significantly more time to perform tasks requiring task switching, searching for stimuli, and arranging them. The data obtained indicate differences in the organization of visual task switching processes in men and women.

Keywords: attention switching, task switching, executive functions, fMRI, sex-related differences, visual stimuli

DOI: 10.1134/S0362119715050084

The ability to implement targeted behaviors and control one's own activity is an important feature of the human being enabling cognitive control of human activity. Executive functions underlie his ability [1, 2]; voluntary task switching (TS), or the ability for conscious and quick shifting of the focus of attention between different tasks, operations, or mental activities [3], is an important component of these functions. The majority of neuroimaging studies of TS point at bilateral dorsolateral prefrontal and parietal areas as the main neural substrate of this process [4–6]. However, the study of brain functioning is not limited to the clarification of the general structure of brain areas involved in the implementation of a certain function; many researchers aim at detecting differences in brain functioning in subjects of different sexes and ages, people suffering from organic or mental diseases [6–9], etc.

Differences between men and women were discovered in a large number of studies addressing brain morphology, cognition, and emotional processes; differences at the neurophysiological and neurochemical levels were detected as well, notwithstanding the apparent overall similarity of certain forms of behavior and results of cognitive activity [7, 8, 10]. For instance, several researchers reported that the posterior part of the corpus callosum is larger in women than in men [8], although other studies did not reveal any differences [11]. According to some reports, the volume of the ventral anterior part of the cingulate gyrus is larger in women than in men [9]. A number of reports stated that the volume of the gray matter in the brain, as well as the ratio between gray and white matter volumes, is higher in women, while the white matter volume is higher in men [12]. Secretion of the male sex hormone testosterone during fetal development was shown to affect the emergence of brain asymmetry [10]. Psychophysiological studies demonstrated that the resting-state functional connectivity correlated differently with risk propensity in men and women [13]. Neuroimaging studies revealed sex-related differences in BOLD response during the assessment of stress level associated with video clip watching and test-taking [14], as well as the difference in hippocampus activation associated with performing spatial tasks [15]. Psychological studies showed sex-related differences in visuospatial tests, speed of perception, properties of attention [7], and other characteristics.

Notwithstanding the large number of studies addressing structural, functional, and psychological features of sex-related differences, neuroimaging studies of TS in men and women are extremely scarce, although psychological studies demonstrate the difference in men's and women's performance in voluntary attention switching. Several studies have shown that women are better at tasks requiring frequent attention switching [7, 16] and demonstrate higher regulatory flexibility [17], while men are better at visuospatial tasks and exhibit greater flexibility in problems related to mental rotation of shapes [7]. We are currently aware of only one functional magnetic resonance imaging (fMRI) study addressing sex-related differences in visuospatial switch task [18]. This study revealed increased activation in the inferior prefrontal cortex, anterior cingulate gyrus, caudate nucleus, and the inferior parietal region of women's brains; no increases in activation were detected in any area of the male brains. Other neuroimaging studies addressing executive functions revealed increased activation in the prefrontal areas of the female brains and the parietal areas of male brains upon working at tasks involving working memory and mental rotation of shapes [19]; tasks related to motor inhibition resulted in increased activation of frontal, parietal, temporal, and thalamic areas of the female brains [20]. These observations suggest different strategies for the fulfillment of the same tasks by men and women.

Thus, neuroimaging studies on executive functions revealed the principal differences in the activation of prefrontal and parietal areas of the brain in men and women; on the other hand, sex-related differences in performance in TS were demonstrated by psychological studies. We assume that comparison of the results obtained in these two types of studies will ensure a more thorough analysis and understanding of the mechanisms of visual attention switching in men and women; in addition, the role of the prefrontal and parietal areas, as well as the possible involvement of other brain areas in these processes can be clarified.

Therefore, the aim of the present study was to analyze the distinctive features of visual TS in men and women using fMRI and psychological tests.

METHODS

Eighty-two subjects 21–48 years of age participated in the study; they all filled out questionnaires on neurological or mental disease. The presence (or absence) of organic brain damage was determined in the T1 and T2 weighted images. A threshold value of 75% correct answers was set to increase the validity of the data. Handedness was defined using the Annett test [21]. The subjects who had organic brain damage (eight subjects), gave less than 75% of correct answers (three subjects), or were left-handed (one subject) were excluded from the study. The final set included 70 subjects of 21–48 years of age: 36 men (average age, 34.83 ± 8.95 years) and 34 women (average age, 32.12 ± 6.6 years). The educational level of the subjects was distributed in the following way: 10% had secondary professional education; 10%, unfinished higher education; 70%, higher education; and 10%, an academic degree. The male (m-group) and female (f-group) subject groups did not differ significantly with respect to age or education level.

All subjects gave written consent for participation in the experiment, data processing, and publication of the results, as required by the Declaration of Helsinki.

Visual Switching Task Used in the fMRI Study

The task consisted of two types of blocks: the experimental block requiring the subjects to switch attention from one condition of the task to another condition and the control block not requiring attention switching and limited to fulfillment of the commands given on the screen. A scheme of an example task is shown in Fig. 1.

Assessment of the shape or number of geometrical figures presented was required of the subject during the experimental block of the task. One or two white geometrical figures were presented on a black background; each presentation was preceded by a cue image defining the assessment criterion. The cue image either showed an empty square or two empty circles. If an empty square was presented to the subject, he or she had to respond according to the shape of the subsequently presented image (square or not), pressing the right button when seeing a square shape and the left button when seeing a non-square shape, regardless of the number of shapes on the screen. If two empty circles were presented to the subject, he or she had to respond according to the number of the shapes presented after the circles, pressing the right button if two objects were presented, or the left button if just one object was presented, regardless of the shape of the objects. The subject had to follow the sequentially presented figures and assess their shape or number according to the preceding cue image. The figures were presented in a pseudorandom order. Every block included three switches of conditions.

The control block consisted of presentation of a triangle pointing to the left or to the right, and the subject had to press the button corresponding to the direction in which the triangle was pointing; that is, the cue to be followed was explicitly presented on the screen. A cross was shown between the consequent triangle presentations.

The subjects were shown the "Sorting" command before each experimental block and the "Direction" command before each control block. The command was presented for 2000 ms and followed by a black screen (for 1000 ms) and the test block. Each figure was presented for 4000 ms, and the cue images in the

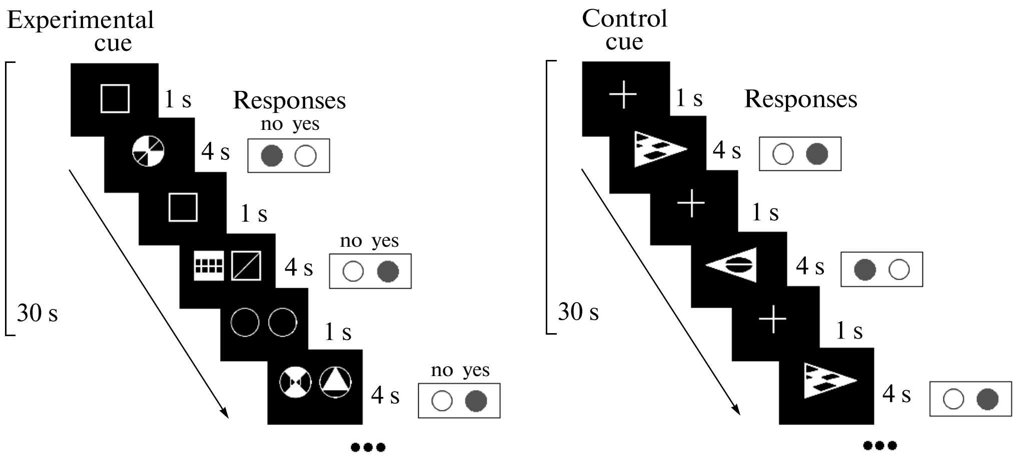

Fig. 1. An example of experimental and control conditions used in the fMRI study.

experimental blocks, as well as the crosses in the control blocks, were presented for 1000 ms. Each block consisted of six shapes. The duration of a block was 30 s. The blocks were presented in a pseudorandom order, with eight blocks for each condition, and a training experimental block at the beginning of the test (this training block was not included into the further data analysis). A cross at the center of the screen was presented for 9 s between blocks and the subjects were instructed just to look at it. The number of left and right button presses was similar both in the experimental and control conditions. The subject had to press the buttons with the left hand, using the index finger to press the right button and the middle finger to press the left button. The duration of the whole task was 12 min and 9 s.

All subjects were trained by performing a short computer task similar to the experimental task prior to the actual experiment. After the subject performed the task correctly, he or she was asked to perform the same task inside a MRI scanner.

The fMRI task for task switching was presented to the subjects in an automatic mode using the E-Prime 1.0 software. The time of reaction to stimuli, as well as the number of correct and incorrect answers, was registered as the subjects performed the task.

Neuropsychological tests for the assessment of memory and executive functions. The Delis–Kaplan test [22]—specifically, the D-KEFS Trail Making Test battery—was used for the assessment of executive functions in the present study.

This test includes five subtests. The main subtest is intended for TS analysis and involves the assessment of cognitive flexibility. It requires the subject to switch between numbers and letters sequentially, with the highest possible speed. The remaining four subtests allow for the assessment of key components required for the fulfillment of a TS task, namely, visual scanning, ordering of numbers, ordering of letters, and a subtest assessing the speed of hand movement upon drawing straight lines. The subjects were asked to recall the Russian alphabet before the letter ordering test, since the knowledge of the alphabet is insufficient in some speakers of Russian.

The time of task completion (in seconds) and the number of mistakes were the parameters used for the assessment of the subjects' performance in the Delis–Kaplan test.

The Wechsler Memory Scale [2] was used to assess auditory and visual memory.

The first and second subtests of this test are intended for the assessment of auditory attention and memory. The subject has to memorize series of numbers (of increasing length) and repeat them in direct or reversed order. The third subtest is used to assess auditory working memory and involves the presentation of a random sequence of letters and numbers. The subject has to name the numbers in the direct order and then name the letters in alphabetical order. The fourth and fifth subtests address visual memory and visual attention. The subject has to remember the sequence of cubes randomly placed on a board and recall it in direct or reversed order.

Performance in the Wechsler test was assessed according to the maximal length of a completely remembered series and the percentage of correct answers.

Each subject was given both fMRI and psychological tests on the same day. Some subjects first took the fMRI test that lasted approximately 30 min, and then took the neuropsychological tests that lasted 30–40 min, some subjects first took the neuropsychological tests and then the fMRI test, and the rest of the subjects fulfilled a part of the neuropsychological tasks prior to the fMRI study and took the remaining tests after the imaging. Breaks of 5–10 min separated fMRI and psychological tests.

Parameters of scanning. The fMRI scans were performed on a MAGNETOM Avanto 1.5T device (Siemens). The T1 MP-RAGE sequence (TR, 1900 ms; TE, 2.91 ms; slice thickness, 1 mm; 176 slices; FoV, 250 mm; reconstruction matrix, 256 × 256; voxel size, 1 × × 1 × 1 mm) was used to construct a sagittal anatomical image. The EPI sequence was used to register the BOLD signal in fMRI (TR, 3000 ms; TE, 50 ms; 35 slices; FoV, 192 mm; reconstruction matrix, 64 × 64; voxel size, 3 × 3 × 3 mm). The total number of measurements in the fMRI study was 241.

Data processing. The data obtained were processed on the individual and group level using the SPM8 software (http://www.fil.ion.ucl.ac.uk/spm/) based on Matlab R2012 (MathWorks, Natick, United States). The sections were oriented parallel to the plane bisecting the frontal and caudal commissures of the brain. Prior to second level statistical analyses, the images were realigned coregistered, segmented, and normalized to the stereotactic template of the Montreal Neurological Institute (MNI-template). Normalized images were smoothed with a Gaussian kernel of 8 mm FWHM. Individual activation maps were constructed using the general linear model. Group maps were produced from the data of individual subject maps using a random effect model. One-sample t test was used to construct the group activation maps, and two-sample t test was used to compare the groups. All the activation clusters identified were presented in MNI coordinates. Statistical thresholds for the analysis of group activation maps in individual groups were set at the voxel level $p < 0.01$, with correction for multiple comparisons, and the significance level for the clusters $p(FWE\text{-}corr)$ was set at $p < 0.001$. The voxel threshold for the comparison of groups was set at $p < 0.001$ (unc.), with a corrected significance threshold for the clusters $p(FWE\text{-}corr)$ at $p < 0.001$. The SPM anatomy toolbox application, version 1.8 [23] was used to characterize the spatial localization and volume of the activated areas. The Brodmann areas were identified using the Talairach Client 2.4.3 software; for this, the MNI coordinates were transformed into Talairach and Tournoux coordinates [24] using GingerALE 2.3.1 software. The Marsbar software [25] was used to assess the contrast values for each group separately and to estimate the difference between groups. The areas of interest for this analysis were selected using the WFU_PickAtlas_3.0.4 software and included the areas mentioned in most reports of studies addressing voluntary switching of attention [26]: the lower frontal gyrus (the triangular part) in the left hemisphere (LH) and the right hemisphere (RH), the middle frontal gyrus of the LH and RH, and the inferior parietal lobule of the LH and RH. Assessment of the connections between the contrast of BOLD signal (the value for experimental conditions minus the value for control conditions) and the results of psychological tests was performed using the SPM8 software with the voxel threshold set at $p < 0.001$ (unc.) and the corrected significance threshold for the clusters $p(FWE\text{-}corr)$ set at $p < 0.01$. Statistical processing of behavioral data (reaction speed and the number of correct and incorrect answers) and the comparison between the degrees of signal increase in the regions of interest were performed using the SPSS 16.0 software. Normal distribution of the data was verified prior to the actual analysis using the Kolmogorov–Smirnov test. Differences between groups were assessed using the Mann–Whitney U-test (for variables not following a normal distribution) or Student's t-test (for variables following a normal distribution).

RESULTS

The distribution of values of almost all the dependent variables deviated from normal, as shown by the results of Kolmogorov–Smirnov test ($p < 0.05$ for all variables), with the reaction speed in D-KEFS subtests 1, 2, and 3 and signal increase in the areas of interest forming an exception ($p > 0.09$).

Group performance in an fMRI TS was assessed first. Both groups generally showed good performance; the average percentage of correct responses in the TS task was 97 for the m-group and 98 for the f-group, although five subjects from the m-group and one subject from the f-group gave less than 90% correct responses. The average percentage of correct responses in the control task was 99 for both groups. The number of subjects who did not make any errors in the TS task was 60% in both groups.

The number of errors and the average reaction speed were then compared between the m-group and the f-group. The number of errors (average rank 35.42 for the m-group and 35.59 for the f-group) in the TS (the Mann–Whitney U-test was 609.0, $p = 0.968$) and in the control task ($U = 572.0$, $p = 0.333$) did not exhibit significant differences between groups.

The "net" time of TS was estimated by subtracting the reaction time for the control block from the reaction time for the experimental block. Average reaction speed (net TS time) values did not exhibit significant difference between groups (m-group: $M = 380.88$, $SD = 185.91$; f-group: $M = 318.55$, $SD = 162.57$); $t = 1.49$, $p = 0.141$. Thus, the data obtained demonstrate the absence of significant difference between the number of errors and average TS time for the two groups of subjects.

The brain areas involved in TS were identified using the assessment of relative difference between the BOLD signals for the two conditions (experimental minus control). Activation clusters with maximal signal intensity observed upon the fulfillment of a TS task in the m-group were located in the inferior and middle frontal gyri (Brodmann area (BA) 9), inferior and middle occipital gyri (BA 18), inferior parietal lobule (BAs 7 and 40), cerebellar cortical areas, supplementary motor area (BA 6) of the LH and RH, precentral

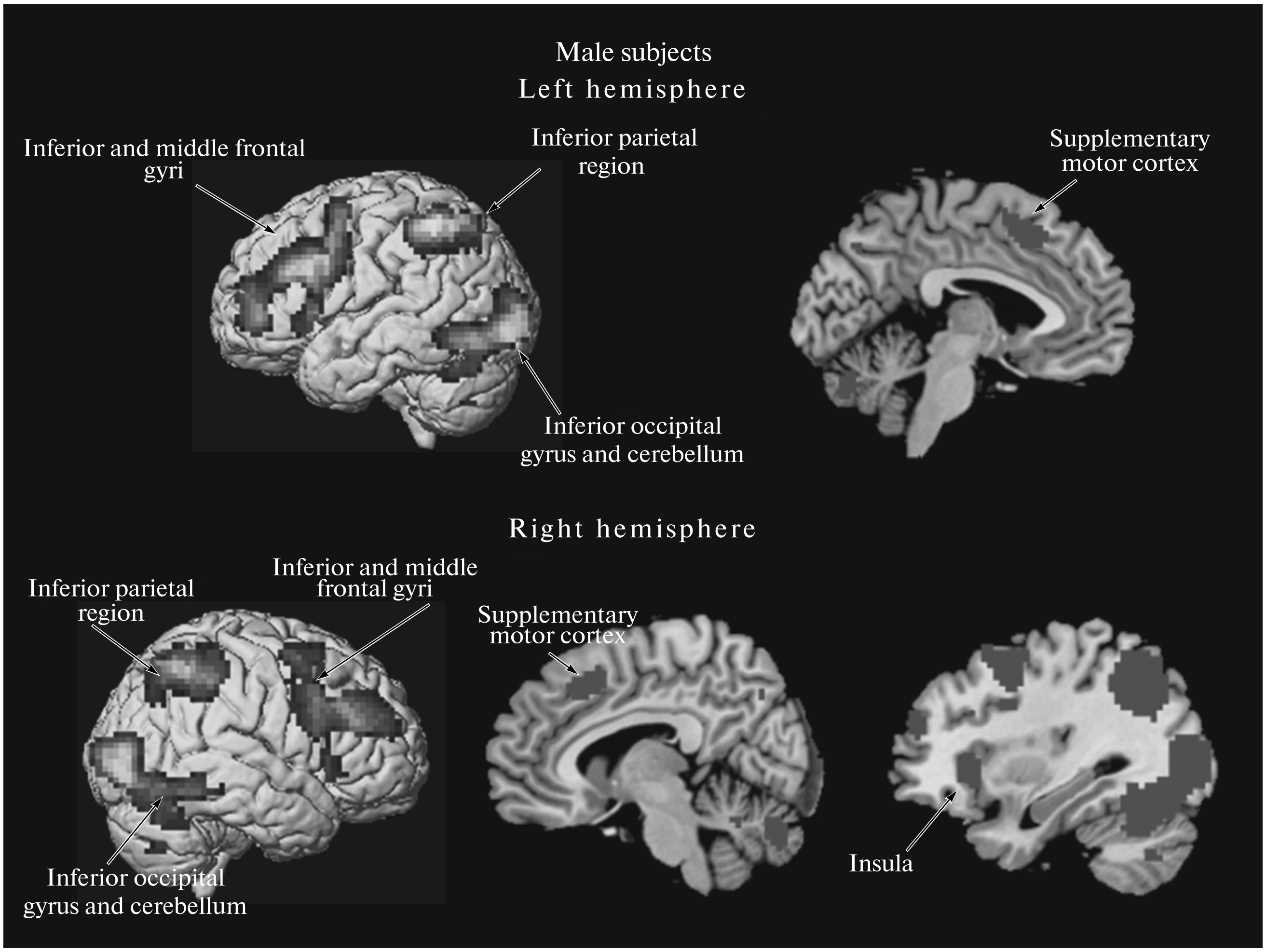

Fig. 2. The results of fMRI analysis in men performing a task switching as compared to fMRI pattern observed under the control condition (voxel level $p < 0.01$, with correction for multiple comparisons; cluster correction $p(FWE\text{-}corr) < 0.001$).

gyrus (BA 6), LH thalamus, and RH insula (BA 13) (Table 1, Fig. 2).

Activation clusters with maximal signal intensity observed upon the fulfillment of a TS task in the f-group were located in the inferior frontal gyrus (BA 9), inferior and middle occipital gyri (BA 18), inferior parietal lobule (BAs 7 and 40), cerebellar cortical areas of the LH and RH, and precentral gyrus (BA 6) of the LH (Table 1, Fig. 3).

The increase of the BOLD signal for the middle frontal gyrus (BAs 9 and 10) of the LH and RH, supplementary motor area (BA 6) and insula of the RH, inferior frontal and precentral gyri (BAs 9 and 6, respectively), and superior and inferior parietal lobules (BAs 7 and 40) of the LH was more pronounced in the m-group than in the f-group (Table 1, Fig. 4). No areas in which the increase of the BOLD signal in the f-group exceeded that observed in the m-group were identified.

Conjunction statistical analysis was performed to identify the areas activated during the accomplishment of the TS task in both groups of subjects. The common activation areas with maximal signal intensity were located in the inferior frontal gyrus (BA 9, 10), inferior parietal lobule (BAs 7 and 40), inferior occipital (BA 18) and precentral (BA 6) gyri, and cortical cerebellar areas of the LH and RH, as well as in the right insula (Table 1). Thus, the pattern of activation of brain areas in the m-group was similar to that observed in the f-group, but the volume of the activation clusters in the dorsolateral prefrontal areas and the insula was higher, and there were additional activation clusters in the supplementary motor area of the LH and RH of male, but not female brains.

The contrast values were calculated for each subject, and the groups were compared using the t-test for independent samples, since the Kolmogorov–Smirnov test showed that these variables followed the normal distribution, and Levin test for the homogeneity of variance revealed the homogeneity of both groups. The signal increase for the m-group significantly exceeded that for the f-group in case of the infe-

Table 1. Activation clusters in brain areas during an fMRI study involving an attention switching task as compared to activation pattern under control conditions

Cluster size (volume in voxels)	*p*(*FWE-corr*)	H	Localization	MNI coordinates {*x*; *y*; *z*}	*Peak T-value*	≈*BA*
m-group						
1216	.000	*L*	*Inferior frontal gyrus*	–45; 29; 25	14.02	9
			Precentral gyrus	–42; 2; 28	12.20	6
			Middle frontal gyrus	–45; 38; 28	11.89	9
1097	.000	*L*	*Inferior occipital gyrus*	–33; –88; –5	14.18	18
			Cerebellum	–27; –58; –29	11.92	–
			Middle occipital gyrus	–27; –94; 4	11.54	18
965	.000	*R*	*Middle occipital gyrus*	30; –85; 4	13.68	18
			Inferior occipital gyrus	36; –85; –2	13.61	18
			Cerebellum	27; –61; –29	10.39	–
878	.000	*R*	*Insula lobe*	33; 23; –2	12.07	13
			Middle frontal gyrus	36; 50; 19	9.29	9
			Inferior frontal gyrus	48; 11; 22	9.20	9
788	.000	*R*	*Inferior Parietal Lobule*	42; –55; 49	12.78	7
			Inferior Parietal Lobule	42; –49; 43	12.71	40
763	.000	*L*	*Inferior Parietal Lobule*	–36; –49; 43	15.52	40
197	.000	*R*	*SMA*	3; 17; 46	10.96	6
		L	*SMA*	–6; 20; 46	9.96	6
18	.000	*L*	*Thalamus*	–12; –19; 16	7.76	–
f-group						
556	.000	*L*	*Middle occipital gyrus*	–30; –88; –2	11.75	18
			Inferior occipital gyrus	–39; –79; –11	11.36	–
540	.000	*R*	*Inferior occipital gyrus*	30; –88; –2	11.47	18
			Cerebellum	36; –67; –29	9.77	–
534	.000	*L*	*Inferior parietal lobule*	–36; –52; 43	12.69	40
321	.000	*R*	*Angular gyrus*	36; –61; 52	10.00	7
			SupraMarginal gyrus	48; –40; 43	8.65	40
303	.000	*L*	*Inferior frontal gyrus*	–45; 29; 25	8.94	9
			Precentral gyrus	–45; 8; 37	8.81	6
32	.000	*R*	*Inferior frontal gyrus*	54; 29; 31	7.65	9
31	.000	*L*	*Cerebellum*	–27; –67; –50	9.94	–
m-group > f-group						
826	.000	*R*	*SMA*	3; 17; 46	5.79	6
			Insula lobe	33; 23; –2	5.26	–
			Middle frontal gyrus	33; 14; 61	5.12	–
223	.000	*L*	*Precentral gyrus*	–39; 2; 31	4.77	6
			Inferior frontal gyrus	–45; 17; 22	4.67	9
			Middle frontal gyrus	–48; 26; 34	3.85	9

Table 1. (Contd.)

Cluster size (volume in voxels)	*p*(*FWE-corr*)	H	Localization	MNI coordinates {*x*; *y*; *z*}	*Peak T-value*	≈*BA*
209	.000	*R*	*Middle frontal gyrus*	36; 47; 31	4.98	9
203	.000	*L*	*Superior Parietal Lobule*	–36; –70; 52	4.26	7
			Inferior Parietal Lobule	–36; –49; 43	4.19	40
160	.000	*L*	*Middle frontal gyrus*	–33; –53; 19	5.10	10
			Conjunction analysis			
674	.000	*L*	*Inferior occipital gyrus*	–33; –88; –5	11.81	18
			Cerebellum	–33; –67; –26	7.23	–
674	.000	*R*	*Inferior occipital gyrus*	36; –86; 0	11.24	18
			Cerebellum	36; –71; –21	8.04	–
544	.000	*L*	*Inferior Parietal Lobule*	–36; –56; 48	12.24	7
431	.000	*R*	*Inferior Parietal Lobule*	42; –55; 49	9.28	40
408	.000	*L*	*Inferior frontal gyrus*	–45; 29; 25	9.85	9
			Precentral gyrus	–45; 5; 40	8.61	6
35	.000	*L*	*Inferior frontal gyrus*	–42; 44; 7	6.32	10
32	.000	*R*	*Precentral gyrus*	42; 5; 28	7.08	6
31	.000	*R*	*Inferior frontal gyrus*	42; 29; 25	6.39	9
14	.000	*R*	*Insula lobe*	33; 23; 1	7.15	–

H, hemisphere; *L*, left hemisphere; *R*, right hemisphere; *BA*, cytoarchitectonic Brodmann area; *p*(*FWE-corr*), threshold level of significance for a cluster; *Peak T-value*, *T* values for the peaks.

rior frontal gyrus of the LH (m-group: M = 0.3053; SD = 0.1577, f-group: M = 0.1844; SD = 0.1402, t = 3.381, p = 0.001) and RH (m-group: M = 0.2011; SD = 0.1914, f-group: M = 0.0782; SD = 0.1366, t = 3.075, p = 0.003); the middle frontal gyrus of the LH (m-group: M = 0.2183; SD = 0.1651, f-group: M = 0. 0762; SD = 0.1438, t = 3.382, p = 0.000) and RH (m-group: M = 0.2747; SD = 0.2032, f-group: M = 0.0894; SD = 0.1533, t = 4.288, p = 0.000); and the inferior parietal lobule of the LH (m-group: M = 0.5558; SD = 0.2638, f-group: M = 0.3576; SD = 0.1791, t = 3.695, p = 0.000) and RH (m-group: M = 0.4883; SD = 0.2682, f-group: M = 0.3138; SD = 0.2619, t = 2.751, p = 0.008).

Differences between the performance of men and women in neuropsychological tests were analyzed using the Mann–Whitney *U*-test on the values of reaction speed in Wechsler subtests 4 and 5 and total number of errors in the Delis–Kaplan test (Table 2); in addition, *t*-test for independent samples was applied to the values of time required to complete Delis–Kaplan subtests 1, 2, and 3 (Table 3).

Significant differences between groups were detected in the TS and the number ordering subtest. The female subjects completed these tests in a significantly shorter time. The difference between the time periods required for completion of the letter ordering test approached the level of significance, with women performing faster in this task as well.

The number of errors and completion time (in seconds) for each subtest of the Delis–Kaplan test along with the percentage of correct answers and the maximal length of a completely remembered series in the Wechsler test were used as the independent variables in the analysis of correlation between BOLD signal contrast and performance in psychological tests. Significant correlations between the BOLD signal and the results (both error number and completion time) of subtest 4 of Delis–Kaplan test intended for the assessment of TS between tasks were detected. If a subject

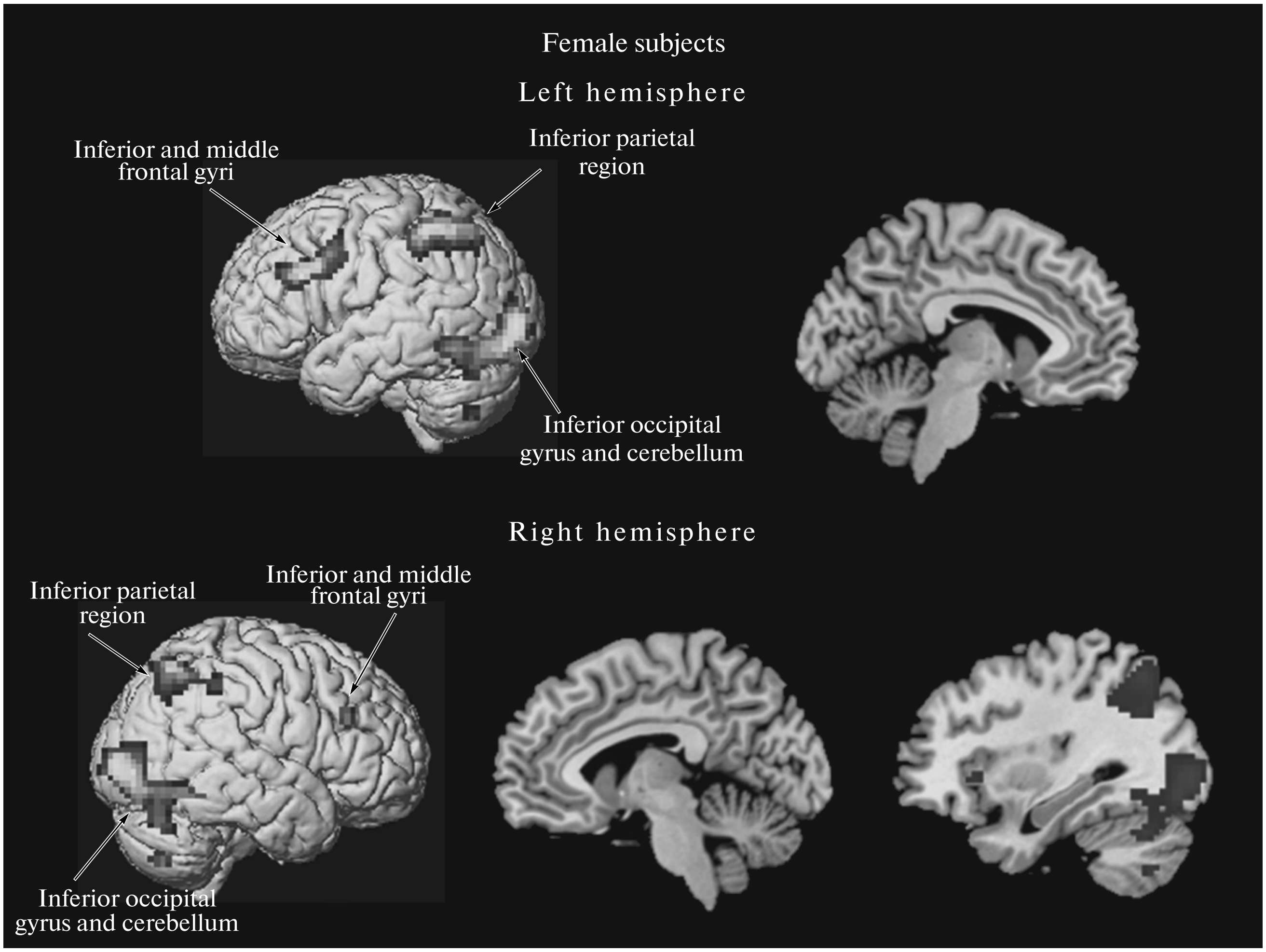

Fig. 3. The results of fMRI analysis in women performing a task switching as compared to fMRI pattern observed under the control condition (voxel level $p < 0.01$, with correction for multiple comparisons; cluster correction $p(FWE\text{-}corr) < 0.001$).

took more time to perform the task, increased activation with maximal signal intensity was detected bilaterally in the middle and inferior frontal gyri, the supplementary motor area on the left, and the medial occipital-temporal gyrus and cerebellum on the right. The increase of the number of errors in the above named task was accompanied by increased activation with maximal signal intensity bilaterally in the middle and inferior frontal gyri, the supplementary motor area, the inferior parietal lobe, the lateral parietal gyri and the cerebellum, as well as in the medial occipital-temporal gyrus of the RH. Correlation with time of completion of subtest 3 (searching for letters and ordering them) was detected as well. Slower completion of the test corresponded to more pronounced activation in the inferior and middle frontal gyri bilaterally, the parietal lobule, and the lateral occipital gyri on the right. Results of the analysis of the correlation between BOLD signal and performance in the above named psychological tests are presented in Table 4. No statistically significant correlations were detected between BOLD signal contrast and performance in other subtests of Delis–Kaplan test or in the Wechsler test. Since the correlation was detected for the letter ordering subtest but not the number ordering subtest, performance quality and completion time for these subtests were compared using statistical analysis. Processing of numbers is automatized to a greater extent than processing of letters, and therefore the difference observed may be explained by the higher level of difficulty of the third subtest. The same number of items was presented in both tests. The Mann–Whitney *U*-test was applied to the number of errors, and the *t*-test for dependent samples was applied to the time of task completion in order to detect differences between the subtests. Significant differences between the results of these two tests were detected: the subjects completed the number ordering test in a significantly shorter time (M(subtest 2) = 30. 66; SD = 9.7, M(subtest B) = 49.9; SD = 13.7, $t = -10.31$, $p = 0.000$), and made significantly less errors (average rank 0 for subtest 2 and 5.5 for subtest 3, $Z = -2.85$, $p = 0.004$).

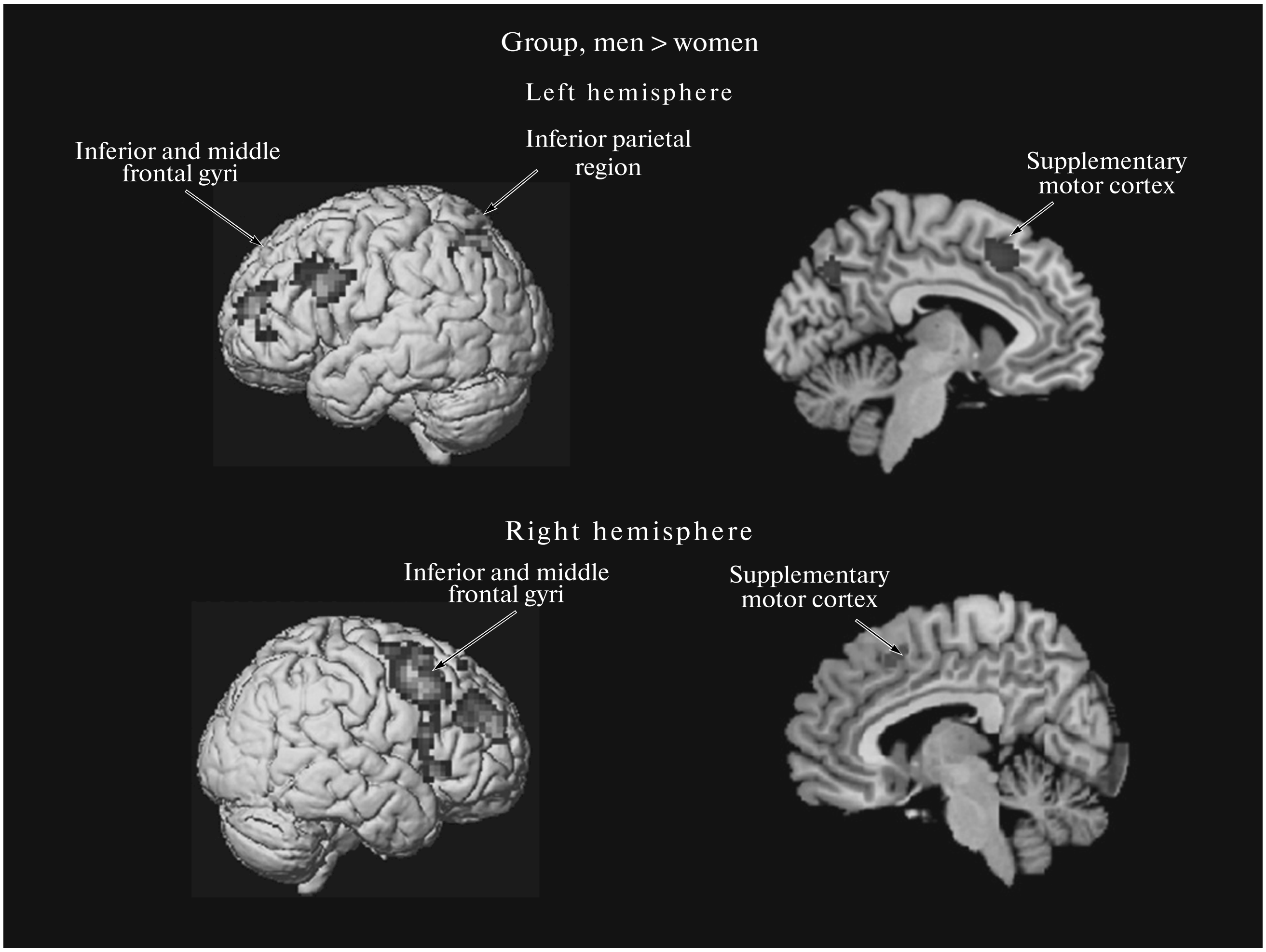

Fig. 4. Differences in BOLD response intensity between the experimental and control conditions, male subjects > female subjects (voxel level $p < 0.001$ (unc.), threshold level for cluster significance set at $p(FWE\text{-}corr) < 0.001$).

Thus, subtest 3 turned out to be less automatized and more difficult for the study subjects.

DISCUSSION

Bilateral activation in dorsolateral prefrontal areas, inferior parietal lobes, and inferior occipital gyri was observed in both groups of subjects in the present fMRI study of visual TS. Similar activation patterns were reported by most neuroimaging studies addressing the switching of visual attention [4–6, 26].

In addition, significant differences in men's and women's performance in a visual TS were revealed by the present study. Significantly more pronounced activation of prefrontal areas, the left parietal lobe, and the right insula of the brain was detected in the male subjects; moreover, activation in the supplementary motor area was observed for the men, but not for the women. Activation of the supplementary motor area for switching was reported previously by another research group [4]. This zone is supposed to be involved in processes requiring a change of the reaction and inhibition of the response to the preceding stimulus [27]; activation of this area was also observed when difficult tasks were offered to the subjects, as well as during the initial stages of learning [28], and therefore the function of this area is not limited to motor tasks [29]. The right insula was also activated by tasks of various types [28]. Note that additional or higher activation of this area was observed in experiments addressing the level of complexity of the tasks [28, 30]. Analysis of the effect of increasing task complexity on brain activity performed by Tregellas et al. [28] revealed increase of activation and the emergence of additional activated areas in the supplementary motor areas, insula, dorsolateral prefrontal areas, thalamus, and striatum. The areas named above were not activated if the task was easy for the subjects [28]. Thus, a higher degree of activation and the recruitment of additional brain areas usually accompany the increase in task difficulty in neuroimaging studies. Some studies also reported the decrease in activation of certain

Table 2. Results of the Mann–Whitney test for the comparison of groups of men and women

	Subtests of Delis–Kaplan test					
	1	2	3	4	4a	5
ARm	36.54	34.5	35.56	39.87	32.58	31.01
ARf	32.46	34.5	33.44	27.95	31.44	37.99
U	508.5	578.0	542.0	361.5	478.0	459.5
p	0.165	1.0	0.473	0.012	0.75	0.146

	Subtests of Wechsler test									
	6	6a	7	7a	8	8a	9	9a	10	10a
ARm	35.69	33.56	38.51	36.03	34.37	31.76	35.33	34.83	37.19	34.66
ARf	34.24	36.58	31.17	33.88	34.64	37.41	33.62	34.15	30.52	33.28
U	569.0	542.0	557.0	467.5	573.0	481.5	548.5	566.0	448.5	537.0
p	0.759	0.526	0.651	0.116	0.953	0.232	0.71	0.886	0.15	0.769

ARm, average rank in the group of male subjects; ARf, average rank in the group of female subjects; *U*, U value for the Mann–Whitney test; *p*, significance level. Variables: 1, number of errors (NE) in a visual scanning task; 2, NE in a number-ordering task; 3, NE in a letter-ordering task; 4, completion time (CT) of a task switching (TS); 4a, NE in a TS; 5, CT for the speed of hand movement; 6, maximal number (MN) of items memorized in the first subtest; 6a, percentage of correct answers (PCA) in the first subtest; 7, MN in the second subtest; 7a, PCA in the second subtest; 8, MN in the third subtest; 8a, PCA in the third subtest; 9, MN in the fourth subtest; 9a, PCA in the fourth subtest; 10, MN in the fifth subtest; 10a, PCA in the fifth subtest.

Table 3. Results of the *t*-test for the comparison of groups of men and women

Scales of Delis–Kaplan subtests	Group of male subjects		Group of female subjects		*t*	*p*
	M	*SD*	*M*	*SD*		
1	17.74	3.5	16.38	2.98	1.75	0.084
2	33.64	10.63	28.47	8.33	2.23	0.023
3	53.01	15.19	46.89	10.84	1.91	0.061

brain areas after training, often accompanied by a decrease in the number of errors and an increase in productivity [31, 32]. The authors assume that the decline of activation after training is related to more efficient information processing.

Our study revealed a correlation between the BOLD signal recorded in fMRI involving a TS and the results of an independent psychological test designed to assess TS and cognitive flexibility. Elevation of the BOLD signal in the dorsolateral prefrontal areas and the supplementary motor cortex was correlated with slower completion of the test and a higher number of errors in the psychological TS. One may assume that more pronounced activation in the brain areas named

Table 4. Activation clusters in brain areas defined by the analysis of correlations between the BOLD signal contrast (experimental condition minus control) and psychological subtest results

Cluster size (volume in voxels)	*p* (*FWE-corr*)	H	Localization	MNI coordinates {*x*; *y*; *z*}	*Peak T-value*	≈*BA*
Increase of time required for completion of Delis–Kaplan subtest 4						
222	.000	*R*	*Middle frontal gyrus*	36; 11; 61	4.40	6
			Inferior frontal gyrus	51; 20; 37	3.89	8
104	.007	*L*	*Middle frontal gyrus*	–42; 20; 37	5.03	9
			Inferior frontal gyrus	–45; 11; 28	4.14	9
94	.012	*L*	*Frontal superior medial gyrus*	0; 23; 40	4.75	32
			SMA	0; 17; 48	4.17	6
88	.015	*R*	*Cerebellum*	27; –79; –17	4.25	–
			Lingual gyrus	18; –82; –11	3.90	–
Increase of the number of errors in Delis–Kaplan subtest 4						
976	.000	*R*	*Lingual gyrus*	18; –85; –11	9.75	–
			Cerebellum	36; –73; –23	5.88	–
439	.000	*R*	*Middle frontal gyrus*	39; 11; 58	8.10	6
			Inferior frontal gyrus	51; 23; 34	5.99	9
402	.000	*L*	*Inferior parietal lobule*	–36; –76; 46	5.44	7
			Middle occipital gyrus	–27; –73; 25	5.35	19
331	.000	*R*	*Middle occipital gyrus*	33; –82; 37	7.25	19
			Angular gyrus	42; –70; 49	6.66	7
320	.000	*L*	*Frontal superior medial gyrus*	–3; 41; 31	5.75	6
		R	*SMA*	6; 17; 46	3.66	32
271	.000	*L*	*Cerebellum*	–33; –67; –41	5.88	–
			Inferior occipital gyrus	–39; –64; –5	4.58	–
259	.000	*L*	*Inferior frontal gyrus*	–48; 23; –5	5.47	47
			Middle frontal gyrus	–39; 56; 4	5.24	10
Increase of time required for completion of Delis–Kaplan subtest 3						
511	.000	*R*	*Inferior frontal gyrus*	51; 17; 34	4.90	9
			Precentral gyrus	36; –4; 49	4.29	6
			Middle frontal gyrus	39; 8; 58	4.26	6
216	.000	*R*	*Lingual gyrus*	18; –82; –14	5.00	–
150	.001	*R*	*Superior Parietal Lobule*	–36; –70; 49	4.64	7
			Middle occipital gyrus	36; –79; 37	3.96	19
112	.005	*L*	*Inferior frontal gyrus*	–45; 11; 28	4.26	9
			Middle frontal gyrus	–36; 17; 34	3.77	9

H, hemisphere; *L*, left hemisphere; *R*, right hemisphere; *BA*, cytoarchitectonic Brodmann area; *p*(*FWE-corr*), threshold level of significance for a cluster; *Peak T-value, T* values for the peaks.

above is evident of higher difficulty and the necessity of using larger brain resources in a TS performed during the fMRI experiment. The correlation between the higher intensity of BOLD signal evoked by a task in fMRI and slower performance in the letter searching and ordering test is probably evident of a lower degree of automaticity in performing this task. Thus, increased activation in the dorsolateral prefrontal area and supplementary motor cortex during a TS observed in men as compared to women may be evident of greater complexity of this task for men and lower automaticity of performing the task.

The results of the fMRI study are consistent with the results of neuropsychological tests that revealed slower completion of TS by men as compared to women. Recording of the time of task completion was the major feature distinguishing this test from the task used in the fMRI study. Women complete item searching and ordering tasks that required focused attention faster than men. This is in accordance with behavioral data reported by other researchers: women were shown to perform better in tasks requiring fast perception of details and frequent attention shifting. Most women were able to increase the speed of completion of tasks requiring focused attention without changes in the accuracy of performance [7, 16]; the level of regulatory flexibility was higher in women than in men [17]. It should be noted that there was no difference in the net time required for the TS in fMRI; this fact may be due to our attempt to reduce the frequency of errors by instructing the subjects to try to give as many correct responses as possible, instead of emphasizing the importance of performing the task quickly.

Thus, men performed more slowly than women in a neuropsychological task requiring fast shifting of attention. On the other hand, fMRI revealed more pronounced activation of the prefrontal regions of LH and RH, left parietal lobe, and right insula, as well as recruitment of additional brain areas, such as the supplementary motor area, in men; this is probably indicative of higher requirements for resources for the fulfillment of tasks of this type by the male brain. The involvement of additional resources may be the reason for the absence of differences in speed and accuracy of the completion of the fMRI task by men and women. However, this hypothesis requires further experimental verification.

It should be noted that the results of a study of sex-related differences in TS reported by Christakou et al. [18] differ from those of the present study. Christakou et al. analyzed the performance of adolescents and adults (13–38 years of age) of either sex in a TS including a spatial component. The subjects had to switch between two dimensions in space: that is, a double-ended arrow, either horizontal or vertical, was presented in the middle of a screen divided into four parts, and the subject had to determine whether the stimulus is in the top or bottom part of the screen or, alternatively, whether the stimulus is in the left or right part of the screen; the arrow served as a cue. That is, a subject performing the task had to switch between two types of conditions and to select the location of the stimulus relatively to one of the two spatial axes by pressing one of the four buttons. Bilateral activation of the lower prefrontal cortex, anterior cingulate, and inferior parietal region was more pronounced in the female participants of the study than in the males, while no areas exhibiting stronger activation in males than in females were detected. The results of Christakou et al. are in good agreement with studies demonstrating that men perform better than women in visuospatial tasks [19, 33]; however, the task used in the present study neither included a spatial component nor required mental rotation or assessment of the location of an item in predetermined coordinates, this providing a possible explanation for the difference in the results of the studies.

Thus, distinctive features of activation of the dorsolateral prefrontal area and supplementary motor cortex, as well as the correlations between the two types of tasks in psychological TS tests are evident of sex-related differences in the organization of TS processes.

The results can be explained using recent research reports: for example, Ingalhalikar et al. [34] found that intrahemispheric connections predominated in the cerebrum of males, while interhemispheric connections predominated in the cerebrum of females; the differences emerged and increased during puberty. Consequently, the authors assumed that the organization of the male brain is adapted to maintaining connections between perception and coordination of actions, and therefore men perform better in spatial tasks. On the other hand, the structural features of the female brain organization provide for efficient connection between the analytical and intuitive modes of information processing, and therefore women perform better in tasks assessing social cognition skills [34]. Neurophysiological studies carried out by a Russian group showed similar results for EEG coherence upon the memorization of dichotically presented information. The processing of a verbal task by men was accompanied by an increase of coherence mostly within the left hemisphere, while in women this process affected both hemispheres. Productivity of mnemonic processes in women was associated with an increase in inter-hemispheric coherence, while in men, the reverse relationship was observed. The authors consider the results to be evidence for different biological roles of interhemispheric coherence in men and women [35].

To summarize, one can assume that more pronounced interhemispheric connections in women (as compared to men) facilitate the processing of multiple tasks requiring the switching and distribution of attention between different tasks involving both hemispheres. Brain organization of this type allows for sparing use of resources due to combined and coordinated implementation of the simultaneous spatial and logical/analytical modes of functioning. In contrast, each hemisphere of the male brain is involved in the processing of isolated components of tasks, and additional resources for accelerated transfer of information from one hemisphere to the other are brought into use if a task requires attention switching and reallocation.

In addition, the sex-related differences in the organization of TS revealed in this study may be associated with structural features of the brain of men and women. For example, sex-related differences in the structure of the parietal region were reported in [36]; the differences correlated with performance in a test requiring mental rotation of objects. The ratio between the volumes of gray and white matter in this region was higher in women, and this parameter was negatively correlated to performance in a mental rotation task. On the other hand, the area of the parietal region was larger in men, and this morphological difference was positively correlated to performance in a mental rotation task. These results confirm the possible existence of a connection between structural differences in brain organization and the distinctive features of behavioral and functional performance of the brain. The differences observed in our study may also be due to different volume, area, and volume ratio of gray and white matter in the brains of men and women, especially in the dorsolateral prefrontal area. However, this assumption requires further experimental verification.

CONCLUSIONS

Bilateral activation in dorsolateral prefrontal areas, inferior parietal lobes, and lower occipital gyri was detected in both men and women performing a visual attention switching task, this being indicative of overall similarity of structural and functional processes providing for voluntary visual TS in persons of different sex. On the other hand, sex-related differences in the functioning of the brain in a voluntary visual attention switching tasks were detected. Men performing at the same level as women exhibited more pronounced activation in prefrontal regions, left parietal lobe, and right insula; bilateral activation of the supplementary motor area was observed in men but not in women. Men were slower in performing a neuropsychological TS when required to give a quick response. Besides, the BOLD signal from dorsolateral prefrontal cortex and supplementary motor area in fMRI combined with a TS was correlated to performance in a psychological TS; a difference between men and women was revealed by these tests. All this suggests the use of more extensive brain resources by men performing a TS, which probably appears more difficult to men and cannot be performed with the same degree of automaticity as observed in women. The data obtained reveal differences in the organization of visual attention switching processes at both behavioral and physiological levels in men and women.

REFERENCES

1. Akhutina, T. and Pylaeva, N., *Preodolenie trudnostei ucheniya. Neiropsikhologicheskii podkhod* (Overcoming Learning Difficulties: A Neuropsychological Approach), St. Petersburg: Piter, 2008.
2. Lezak, M., Howieson, D., and Loring, D., *Neuropsychological Assessment* Oxford: Oxford University Press, 2004, 4th edition.
3. Miyake, A., Friedman, N.P., Emerson, M.J., et al., The unity and diversity of executive functions and their contributions to complex “frontal lobe” tasks: a latent variable analysis, *Cogn. Psychol.*, 2000, vol. 41, p. 49.
4. Witt, S.T. and Stevens, M.C., Overcoming residual interference in mental set switching: neural correlates and developmental trajectory, *NeuroImage*, 2012, vol. 62, p. 2055.
5. Kim, C., Johnson, N.F., and Gold, B.T., Common and distinct neural mechanisms of attentional switching and response conflict, *Brain Res.*, 2012, vol. 1469, p. 92.
6. Gold, B.T., Kim, C., Johnson, N.F., et al., Lifelong bilingualism maintains neural efficiency for cognitive control in aging, *J. Neurosci.*, 2013, vol. 33, no. 2, p. 387.
7. Il’in, E.P., *Pol i gender* (Sex and Gender), Moscow, 2010.
8. Kovyazina, M.S., *Neiropsikhologicheskii analiz patologii mozolistogo tela* (Neuropsychological Analysis of Pathology of the Corpus Callosum), Moscow: Genezis, 2012.
9. Mann, S.L., Hazlett, E.A., Byne, W., et al., Anterior and posterior cingulate cortex volume in healthy adults: effects of aging and gender differences, *Brain Res.*, 2011, vol. 1401, p. 18.
10. Cahill, L., Why sex matters for neuroscience, *Nat. Rev. Neurosci.*, 2006, vol. 7, p. 477.
11. Luders, E., Toga, A.W., and Thompson, P.M., Why size matters: differences in brain volume account for apparent sex differences in callosal anatomy: the sexual dimorphism of the corpus callosum, *NeuroImage*, 2014, vol. 84, p. 820.
12. Cosgrove, K.P., Mazure, C.M., and Staley, J.K., Evolving knowledge of sex differences in brain structure, function, and chemistry, *Biol. Psychiatry*, 2007, vol. 62, no. 8, p. 847.
13. Zhou, Y., Li, S., Dunn, J., et al., The neural correlates of risk propensity in males and females using resting-state fMRI, *Front. Behav. Neurosci.*, 2014, vol. 8, p. 1.
14. Lee, M.R., Cacic, K., Demers, C.H., et al., Gender differences in neural-behavioral response to self-observation during a novel fMRI social stress task, *Neuropsychologia*, 2014, vol. 53, p. 257.
15. Persson, J., Herlitz, A., Engman, J., et al., Remembering our origin: gender differences in spatial memory are reflected in gender differences in hippocampal lateralization, *Behav. Brain Res.*, 2013, vol. 256, p. 219.
16. *Voprosy prakticheskoi psikhodiagnostiki* (Psychodiagnostic practice), Obozov, N.N, Ed., Leningrad: Leningr. Gos. Univ., 1984.
17. Sharova, E.V., Shendyapina, M.V., Boldyreva, G.N., et al., Individual variation of fMRT responses to eye

opening, motor, and speech tests in healthy subjects, *Hum. Physiol.*, 2015, vol. 41, no. 1, p. 1.

18. Christakou, A., Halari, R., Smith, A.B., et al., Sex-dependent age modulation of frontostriatal and temporo-parietal activation during cognitive control, *NeuroImage*, 2009, vol. 48, p. 223.
19. Weiss, E.M., Ragland, J.D., Brensinger, C.M., et al., Sex differences in clustering and switching in verbal fluency tasks, *J. Int. Neuropsychol. Soc.*, 2006, vol. 12, p. 502.
20. Garavan, H., Hester, R., Murphy, K., et al., Individual differences in the functional neuroanatomy of inhibitory control, *Brain Res.*, 2006, vol. 1105, p. 130.
21. Bizyuk, A.P., *Kompendium metodov neiropsikhologicheskogo issledovaniya* (A Compendium of Neuropsychological Research Methods), St. Petersburg: Rech', 2005.
22. Kaplan, E., Fein, D., Morris, R., and Delis, D.C., *The WAISR as a Neuropsychological Instrument.*, New York: The Psychological Corporation, 1991.
23. Eickhoff, S.B., Stephan, K.E., Mohlberg, H., et al., A new SPM toolbox for combining probabilistic cytoarchitectonic maps and functional imaging data, *Neuroimage*, 2005, vol. 25, p. 1325.
24. Talairach, J. and Tournoux, P., *Co-planar Stereotaxic Atlas of the Human Brain*, Stuttgart: Thieme, 1998.
25. Brett, M., Anton, J.L., Valabregue, R., and Poline, J.B., *Region of interest analysis using an SPM toolbox [abstract]. Presented at the 8th International Conference on Functional Mapping of the Human Brain, June 2–6, 2002, Sendai, Japan.*, Available on CD-ROM in *NeuroImage*, vol. 16, no. 2.
26. Wager, T.D., Jonides, J., and Reading, S., Neuroimaging studies of shifting attention: a meta-analysis, *NeuroImage*, 2004, vol. 22, p. 1679.
27. Crone, E.A., Wendelken, C., Donohue, S.E., and Bunge, S.A., Neural evidence for dissociable components of task-switching, *Cereb. Cortex*, 2006, vol. 16, p. 475.
28. Tregellas, J.R., Davalos, D.B., and Rojasa, D.C., Effect of task difficulty on the functional anatomy of temporal processing, *NeuroImage*, 2006, vol. 32, p. 307.
29. Boldyreva, G.N., Sharova, E.V., Zhavoronkova, L.A., et al., Structural and functional features of the brain in healthy people accomplishing and imagining motor tasks (EEG and fMRI studies), *Zh. Vyssh. Nervn. Deyat. im. I.P. Pavlova*, 2013, vol. 63, no. 3, p. 316.
30. Dunst, B., Benedek, M., Jauk, E., et al., Neural efficiency as a function of task demands, *Intelligence*, 2014, vol. 42, no. 100, p. 22.
31. Vartanian, O., Jobidon, M.E., Bouak, F., et al., Working memory training is associated with lower prefrontal cortex activation in a divergent thinking task, *Neuroscience*, 2013, vol. 236, p. 186.
32. Bless, J.J., Westerhausen, R., Kompus, K., et al., Self-supervised, mobile-application based cognitive training of auditory attention: A behavioral and fMRI evaluation, *Internet Interv.*, 2014, vol. 1, no. 3, p. 102.
33. Hugdahl, K., Thomsen, T., and Ersland, L., Sex differences in visuo-spatial processing: an fMRI study of mental rotation, *Neuropsychologia*, 2006, vol. 44, p. 1575.
34. Ingalhalikar, M., Smith, A., Parker, D., et al., Sex differences in the structural connectome of the human brain, *Proc. Natl. Acad. Sci. U.S.A.*, 2014, vol. 111, no. 2, p. 823.
35. Vol'f, N.V., Razumnikova, O.M., Bryzgalov, A.O., et al., Neurophysiological foundations of sex-related differences in hemispheric organization of selective attention and verbal memory, *Byul. SO RAMN*, 2004, no. 2, p. 82.
36. Koscik, T., O'Leary, D., Moser, D.J., et al., Sex differences in parietal lobe morphology: relationship to mental rotation performance, *Brain Cogn.*, 2009, vol. 69, no. 3, p. 451.

Translated by S. Semenova