Executive processes and motivation are two components that determine goal-directed behaviors. Several findings suggest that distinct regions of the prefrontal cortex play specific roles in these components. In particular, the dorsolateral part of the prefrontal cortex (DLPFC) appears to be involved in executive processes responsible for working memory (Fuster 1997; Tranel, Anderson, & Benton 1994), whereas the ventral portion of the prefrontal cortex (orbitofrontal cortex; OFC) seems to be associated with emotion and motivation (e.g., Elliott, Newman, Longe, & Deakin 2003; for a review see Rolls 2004).

There is growing body of research emphasizing the idea that executive processes and motivation overlap and interact. Overall these researches indicate that interactions between motivation and executive functions are implemented by top–down modulations from the DLPFC to lower-level (e.g., visual) areas (Gazzaley et al. 2007; Krawczyk, Gazzaley, & D’Esposito, 2007). However, having evidence that motivation can influence top–down control, it is important to determine how the reward system neural circuitry influences DLPFC systems thought to mediate top–down control. There are numerous possible sources of motivational influence upon cognitive control, but perhaps the most likely region responsible for translating potential value into attentional enhancement is the OFC. This region has been implicated in the processing of reward value (O’Doherty et al., 2001; Rolls 2004) and primate neurophysiological studies indicate that the OFC may relay motivationally significant information to the DLPFC (e.g., Wallis & Miller 2003). Thus, several authors have suggested that motivation and executive processes are integrated via connections between the OFC and DLPFC (e.g., Hikosaka & Watanabe 2000). Some support for this hypothesis is provided by two recent neuroimaging studies in humans (Gilbert & Fiez 2004; Pochon et al. 2002). In these studies, working memory tasks were performed with reward values dependent on the level of performance (i.e., subjects were given variable monetary rewards for correct performance). The results indicated that the DLPFC was activated by working memory tasks and that this region, together with the OFC areas, showed changes in activity in the context of monetary reward. However, in these studies the typical statistical approach was employed, aimed at functional segregation of distinct areas of activation and deactivation (change distribution analysis, SPM). This approach precludes determination of the “effective connectivity”, which can be defined as the influence of the activity of one cortical region on another (McIntosh et al. 1994). “Effective connectivity” may be measured by structural equation modeling (SEM, or path analysis) of fMRI data within specified constraints.
based on the consideration of anatomical connectivity and the previously recognized linkage between distinct brain areas (Büchel & Friston 2000; Chaminade & Fonlupt 2003). This technique seems to be an appropriate way to determine the influence of motivational context on executive functions. So far, there have been no effective connectivity studies investigating such an influence. Our study was designed to address this issue: we used fMRI and SEM to investigate the effective connectivity between prefrontal regions supporting motivational influence on executive functions.

Sixteen healthy volunteers (all men, mean age 27.6 years; range = 24–33 years) with no history of neurological or psychiatric disease participated in the study. All were right-handed native Polish speakers. The purpose and risks of the study were explained to all subjects who gave their written informed consent. All procedures were approved by the local Ethical Committee (Warsaw Medical University, Poland).

During the fMRI investigation, participants performed a letter variant of the 2-back working memory task and a simple vigilance task (0-back) as a control. The stimuli were sequences of white uppercase letters on a black background, presented centrally in pseudorandom order. The letters (Arial Bold font; size, 32 points) were selected from a set containing 17 consonants (B, C, D, F, G, H, J, K, M, N, P, R, S, T, W, Z). The V and Q consonants were not used, since they are very rarely used in the subjects’ native script of Polish. Stimuli were back-projected from a multimedia projector (DLP Data Projector NEC LT 265 G) on a screen located about 3 m away from the magnet. Stimulus presentation time was 500 ms with an interstimulus interval of 2500 ms. During the interstimulus interval the blank black screen was presented. In the 0-back task, subjects had to identify the target letter “X”, with all other letter stimuli counted as non-targets. To perform the 2-back task, subjects had to identify a target as any letter that was identical to the one that was presented two stimuli previously, with all other letters counted as non-targets. Subjects were instructed to respond to each stimulus with their right index finger using a two-button response pad, by pressing the left button to signal targets (approximately 33% of the stimuli for both the 0-back and 2-back tasks) and the right button to signal non-targets. Before scanning, the subjects were trained on a version of the task designed for use outside the scanner.

The 2-back and 0-back tasks were performed under two reinforcement conditions. The “high-motivation” condition involved the probability of winning a certain amount of money, whereas the “low-motivation” condition was not associated with monetary reinforcement. Subjects performed two experimental runs: one under “high-” and one under “low-motivation” conditions. In each run, the two tasks were presented in a blocked design, alternating three 30-second blocks of the 0-back task (10 trials per block) with three 30-second blocks of the 2-back task (10 trials per block). Both runs began with the 0-back task. At the end of first run, subjects saw the word PAUSE for approximately 20 s before the second run began, providing a rest period. Each block was preceded by a 3 s presentation of an instruction panel giving information regarding the type of task to be performed (0-back or 2-back) and any reward value of the forthcoming run. Except a 3-second instruction period, no delay was provided between blocks. The symbols “100” or “0” indicated that the run would either be highly rewarded (“100”) or would not be rewarded (“0”) for correct responses. The symbol “100” also entailed a risk of losing points for incorrect responses. Subjects were not informed about the precise amount of money associated with the symbol (“100”) to avoid the mental calculation of their putative gains or losses but they were told that the more accurate their responses, the higher the reward. Subjects were informed in advance that after the study they would receive actual remuneration based on the total number of points accumulated throughout the experiment. They were instructed that they could earn up to 500 PLN (about 200 US dollars) and that they should try to win as much money as possible.

Response accuracy and reaction times were separately compared between conditions by a t-test for independent samples. No significant effects of motivation on response accuracy and reaction time were observed.

Functional magnetic resonance images were acquired using a 1.5 T Phillips Gyroscan NT equipped with a 4-channel array coil. EPI images sensitive to BOLD contrast with 16 contiguous transverse slices of 7 mm thickness with 0.5 mm gap were obtained (TR = 3000 ms, TE = 50 ms, flip angle = 90°. Matrix size was 64 x 64 pixels with in-plane resolution of 3.75 x 3.75 mm and a field of view of 240 mm). The fMRI scans were motion corrected, spatially normalized, co-registered and 8-mm smoothed with a Gaussian filter. Low frequency respiratory and cardiac aliasing was removed using a high-pass filter with a cutoff of 128 s. Functional data was analyzed on an individual level with a general linear model using the experimental conditions involved with the canonical hemodynamic response function (Frackowiak, Friston, Frith, Dolan, & Mazzotta 1997). Statistical analysis was performed with SPM2 software (Wellcome Institute, London) and the results were transformed into Talairach’s coordinates using a nonlinear transformation (http://www.mrc-cbu.cam.ac.uk/Imaging/minispace.html).

For SEM (path analysis), time series from the most significant activated pixels in regions referred to the model were extracted. This was done because there is evidence that selecting the most significant activated pixels is a reliable summary measure of condition-specific effects (Goncalves & Hall, 2003). Time course signals were normalized for each subject and signal outliers exceeding two standard deviations were removed (Schlosser, Gesierich, Kaufmann, Vuorcevic, & Stoeter, 2003). For each region, a single time series was defined by the first eigenvector of all the voxel time series. Eigenvectors from each subject and from each location were concatenated into a condition matrix for SEM and subsequent comparisons between conditions.

The PFC regions were included in the model, either due to their importance in executive control (the DLPFC; BA 9, 46) or their putative role in motivation and emotion (the OFC; BA 11, 47). While additional PFC regions, such as the anterior cingulate cortex or frontal pole, could also have been included based on recent reports (Gilbert & Fiez 2004; Pochon et al. 2002; Taylor et al. 2004), we focused on this more limited region set to ensure parsimony (model simplicity), and also to directly test a previously postulated model of the interaction between the OFC and DLPFC (Hikosaka & Watanabe 2000). Furthermore, given that: (1) the OFC consists of the gyrus rectus medially (medial OFC) and orbital gyril laterally (lateral OFC); (2) the medial and lateral portions of the OFC are characterized by different patterns of connections with cortical and subcortical structures (Barbas & Pandya 1989; Carmichael & Price 1996; Cavada, Compañy, Tejedor, Cruz-Rizzolo, & Reinoso-Suárez 2000); and (3) they may play distinct roles in motivational control of goal-directed behavior (Morecroft, Geula, & Mesulam 1992), the lateral OFC and medial OFC in the left and right hemisphere were included separately into the model.

The path model used for SEM was comprised of connections between lateral OFC, medial OFC, and DLPFC regions in the left and right hemispheres. Although there is no evidence in the literature for strong direct anatomical connections between the OFC and contralateral DLPFC areas, we decided to include these connections in the model because previous neuroimaging studies (e.g., Harrison et al. 2005) indicated functional integration of these regions.

Modeling was performed using Amos 4.0 (SmallWaters Corp., USA) applying a maximum likelihood algorithm for estimating path coefficients. Parameters were estimated in SEM by minimizing the difference between the observed covariance and those
implied in the model. The resulting path coefficients represent the change of activity of a target area for a unit change in activity of a source area (Bollen 1988). We used the “stacked model” approach whereby the patterns of effective connectivity in the two conditions could be directly compared. This included the comparison of a free model, in which all connections were allowed to vary between conditions, with a restricted model, in which a given connection was forced to be equal for the two conditions (Schlosser et al. 2003). The comparison of models was done by subtracting the $\chi^2$ value obtained for the constrained model, from the $\chi^2$ value obtained for the free model. This results in a difference $\chi^2$ diff with one degree of freedom.

Table 1 gives a detailed account of the individual path coefficients and $\chi^2$ diff-values in the “low-motivation” and “high-motivation” conditions. We found that experimental data fit accurately the model $[\chi^2(4) = 2.102; P = 0.717]$. The path analysis suggests that only the connection from the right lateral OFC to left DLPFC shows condition-dependent changes in both strength $[\chi^2(1) = 8.27; P = 0.004]$ and sign, with a positive influence in the low-motivation condition and a negative influence in the high-motivation condition.

The aim of the present study was to test the hypothesis that motivation and executive functions are integrated via connections between the OFC and DLPFC. In line with this hypothesis, condition-dependent changes in effective connectivity between the OFC and left DLPFC were observed. As the left DLPFC mediates in the executive component of a letter version of the 2-back working memory task (e.g., Binder & Urbanik 2006), our results suggest that the changes seen in the interactions between OFC regions and the left DLPFC reflect motivational influence on executive functions. This suggestion fits well with previous observations. For example, electrophysiological investigations in monkeys showed that a population of DLPFC neurons, responding to the cognitive aspects of a working memory task, also has its activity modulated by a reward associated with the task (Hikosaka & Watanabe, 2000). Moreover, an fMRI study in humans (Pochon et al. 2002) indicated that the left DLPFC was not only activated by the executive aspects of the n-back working memory task but was also modulated by changes in the reward value. These authors hypothesized that the signal modulating the DLPFC activities originates from areas in the OFC which are thought to provide a contextual value to the ongoing task. Our results, showing that the OFC modulates the activity of the DLPFC, corroborate this view.

While considering the involvement of the OFC in motivational control of executive functions, it is important to appreciate that the medial and lateral OFC regions in the two hemispheres are differentially involved in the expression of motivated behavior (e.g., O’Doherty et al. 2001). In our study, only the connection between the right lateral OFC and left DLPFC showed a significant condition-dependent change in the strength of influence conveyed through the pathway. It could be suggested, therefore, that just this change represents a functional correlate of motivational influence on executive functions. This view would correspond with mounting evidence that the right OFC plays a crucial role in functions tied to the OFC, such as decision making or emotional processing (e.g., Tranel, Bechara, & Denburg 2002).

The results of path analysis showed that the right lateral OFC positively influenced the left DLPFC activity in the low-motivation condition, and negatively in the high-motivation condition. This suggests that, in the low-motivation condition, the right lateral OFC activates the left DLPFC, whereas in the high-motivation condition the right lateral OFC exerts an inhibitory effect on the left DLPFC. Although this is a rather unexpected result of our study, it fits well with recent fMRI data showing that the right lateral OFC is involved in the experience of psychological stress (Wang et al. 2005). As the high-motivation condition involved an increased level of the stress compared with the low-motivation condition, an inhibitory effect between the right lateral OFC and the left DLPFC that was observed in the high-motivation condition could reflect the stress-induced attenuation of executive functions.

On the other hand, studies involving patients with brain lesions (Tranel et al. 2002) and functional neuroimaging (O’Doherty et al. 2001; Thut et al. 1997) suggested that the right and left OFC regions are crucially involved in punishment-related and reward-related affects, respectively. The present study does not attempt to decompose motivational functions into reward and punishment, although the “high-motivation” condition used encompasses both functions. It seems possible, therefore, that a shift in interactions from positive to negative in the network including right OFC regions and the left DLPFC may reflect the effect of punishment on executive functions, whereas the increase in positive interactions in the network composed of the left OFC and DLPFC may reflect the effect of expected reward. Further studies, using punishment and reward separately, are needed to determine whether the right lateral OFC plays a more general role in motivation or, rather, the right and left OFC are differentially involved in the punishing and rewarding aspects of motivational influence on executive functions. Evidence supporting one or the other hypothesis will enhance our understanding of the interplay between motivation and working memory.

### Table 1

<table>
<thead>
<tr>
<th>Path</th>
<th>Path coefficient</th>
<th>Low-motivation</th>
<th>High-motivation</th>
<th>$\chi^2$ diff</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>R LOFC → L MOFC</td>
<td>0.07</td>
<td>-0.49</td>
<td>1.82</td>
<td>0.178</td>
<td></td>
</tr>
<tr>
<td>R MOFC → L MOFC</td>
<td>0.26</td>
<td>0.38</td>
<td>0.09</td>
<td>0.768</td>
<td></td>
</tr>
<tr>
<td>L LOFC → L LOFC</td>
<td>-0.23</td>
<td>0.31</td>
<td>3.67</td>
<td>0.055</td>
<td></td>
</tr>
<tr>
<td>L LOFC → L DLPFC</td>
<td>0.24</td>
<td>0.25</td>
<td>0.02</td>
<td>0.887</td>
<td></td>
</tr>
<tr>
<td>R MOFC → L DLPFC</td>
<td>0.18</td>
<td>-0.19</td>
<td>1.65</td>
<td>0.199</td>
<td></td>
</tr>
<tr>
<td>L MOFC → L DLPFC</td>
<td>0.13</td>
<td>0.52</td>
<td>1.37</td>
<td>0.242</td>
<td></td>
</tr>
<tr>
<td>R MOFC → L DLPFC</td>
<td>0.65</td>
<td>-0.35</td>
<td>8.27</td>
<td>0.004</td>
<td></td>
</tr>
<tr>
<td>L MOFC → R MOFC</td>
<td>-0.07</td>
<td>-0.04</td>
<td>0.03</td>
<td>0.858</td>
<td></td>
</tr>
<tr>
<td>R LOFC → R DLPFC</td>
<td>-0.20</td>
<td>0.04</td>
<td>1.08</td>
<td>0.299</td>
<td></td>
</tr>
<tr>
<td>R MOFC → R DLPFC</td>
<td>0.02</td>
<td>0.10</td>
<td>0.38</td>
<td>0.539</td>
<td></td>
</tr>
<tr>
<td>L DLPFC → R DLPFC</td>
<td>1.04</td>
<td>0.87</td>
<td>0.10</td>
<td>0.754</td>
<td></td>
</tr>
<tr>
<td>L LOFC → R DLPFC</td>
<td>0.12</td>
<td>-0.05</td>
<td>0.47</td>
<td>0.491</td>
<td></td>
</tr>
</tbody>
</table>

The sign of a path coefficient (positive or negative) reflects the sign of the covariance relationship between components of the network. A positive path coefficient means that a unit increase in the activity measure of one structure leads to a direct increase in the activity measure of structures it projects to, proportional to the size of the coefficient. Conversely, a negative path coefficient means that an increase in the activity measure in one structure leads to a direct, proportional decrease in the activity measure of structures it projects to.

L DLPFC, left dorsolateral prefrontal cortex; R DLPFC, right dorsolateral prefrontal cortex; L LOFC, left lateral orbitofrontal cortex; R LOFC, right lateral orbitofrontal cortex; L MOFC, left medial orbitofrontal cortex; R MOFC, right medial orbitofrontal cortex.
Fig. 1. Path diagrams from the casual analysis using structural equation modeling of fMRI data obtained during performance of the verbal 2-back working memory task under (A) “low-motivation” and (B) “high-motivation” conditions. Regional variables are displayed as rectangles and interregional connections are represented by arrows (DLPFC, dorsolateral prefrontal cortex; LOFC, lateral orbitofrontal cortex; MOFC, medial orbitofrontal cortex; L left; R, right). Positive path coefficients are represented as solid arrows, and negative as dashed arrows. Values for the gradient of path coefficients are given in the legend at the bottom.

References


