The frontopolar cortex mediates event knowledge complexity: a parametric functional MRI study

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Event knowledge is organized on the basis of goals that enable the selection of specific event sequences to organize everyday life activities. Although the medial prefrontal cortex represents event knowledge, little is known about its role in mediating event knowledge complexity. We used functional MRI to investigate the patterns of brain activation while healthy volunteers were engaged in the task of evaluating the complexity (i.e. numbers of events) of daily life activities selected on the basis of normative data. Within a left frontoparietal network, we isolated the medial frontopolar cortex as the only region that showed a linear relationship between changes in the blood oxygen level-dependent signal and changes in event knowledge complexity. Our results specify the importance of the medial frontopolar cortex in subserving event knowledge that is required to build and execute complex behavior. ***NeuroReport*** **20:1093–1097 © 2009 Wolters Kluwer Health | Lippincott Williams & Wilkins.**

NeuroReport 2009, **20**:1093–1097

Keywords: frontopolar cortex, hierarchy, humans, prefrontal cortex, sequence

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Received 7 March 2009 **accepted** 13 May 2009

Introduction

Event knowledge is sequentially and hierarchically organized on the basis of goals that enable the selection of specific event sequences. For example, an activity with the goal 'get ready for work' consists of a sequence of events such as 'waking up', 'getting out of bed', 'using the bathroom', 'taking a shower', 'getting dressed', 'eating breakfast', etc. Within this event sequence, subgoals with smaller segments of event sequences are hierarchically embedded. For example, the subgoal activity 'taking a shower' consists of a sequence of events such as 'undressing clothes', 'entering the shower', 'turning on the shower', etc. In the given example, the activity 'get ready for work' would be considered more complex than the activity 'taking a shower', as the number of related events to achieve the goal is greater.

Event knowledge provides the underlying structure for setting goals, making plans, and performing daily life activities [1]. Clinical observations show that the prefrontal cortex (PFC) is essential for goal-directed behavior such as carrying out plans, controlling a course of actions, or organizing everyday routines [2]. Functional neuroimaging studies provide further evidence that the PFC is involved in mediating event knowledge [3–5]. In particular, the medial PFC, which is phylogenetically and ontogenetically older than the lateral PFC, is able to represent abstract 'predictable' event sequences compared with frequently modified event sequences that are preferentially represented in the lateral PFC [6,7].

However, little is known about the exact role of the medial PFC in mediating event knowledge complexity. On the basis of our structural and temporal representation binding theory [8], we assume that the dorsomedial PFC represents abstract dynamic summary representations that give rise to event goal knowledge by binding with regions in the posterior cerebral cortex. Particularly, we argue that as one moves more rostrally to the medial frontopolar cortex, progressively more complex event goal knowledge is represented that guides behavior over progressively longer temporal intervals. This goal pathway expands from the premotor cortex to the medial frontopolar cortex and is required for the storage and specification of complex event goal knowledge such as 'driving to work' as well as coding the concrete instantiation of a particular sequence of neuromuscular outputs. If this proposed goal pathway exists, then variation in complexity should be closely linked to the brain regions selected during tasks that require retrieval of daily life activities. In this study, we used an event-related parametric functional MRI (fMRI) paradigm to investigate the patterns of brain activation when healthy volunteers were engaged in evaluating the complexity (i.e. number of events) of daily life activities selected on the basis of normative data. We predicted that

0959-4965 © 2009 Wolters Kluwer Health | Lippincott Williams & Wilkins DOI: 10.1097/WNR.0b013e32832e7ea5

the variation of complexity in daily life activities should be reflected in the pattern of medial frontopolar cortex activation.

Materials and methods

Participants

Eighteen right-handed healthy native English speakers (nine women; mean ± SD, age 28.3 ± 5.7 years; education level 17.3 ± 2.2 years) participated for financial compensation in the fMRI experiment. None of the participants had a history of medical, psychiatric, or neurological diagnoses, and were not taking any medication. Informed consent was obtained according to procedures approved by the National Institute of Neurological Disorders and Stroke Institutional Review Board.

Stimuli

In a prestudy, 40 participants (17 women, age 26.0 ± 6.1 years, education level 15.7 ± 2.0 years) rated 114 daily life activities chosen from previous studies [9,10]. Participants were asked to rate the complexity and emotion for each daily life activity on a Likert scale: complexity in terms of the number of events involved in the activity (1 = few events, 7 = many events) and emotion in terms of whether the activity has a positive or negative emotional association (1 = very negative, 7 = very positive). For the fMRI experiment, 66 daily life activities were chosen that varied parametrically on complexity ratings from low (e.g. writing your signature) to high (e.g. buying a car). The complexity ratings did not correlate with the emotion ratings ($r = 0.17$, $P = 0.162$) and the word length ($r = -0.19$, $P = 0.112$) for the stimuli.

Procedure

An experimental condition (complexity task) and a control condition (font task) were used. For the complexity task, participants were induced to access stored representations of daily life activities, whereas the font task served as a baseline controlling for display, motor responses, and attentional mechanisms. Participants were first trained on a separate set of stimuli to familiarize them with the experiment. Stimulus presentation was controlled by the ERTS (Experimental Run Time System, Berisoft Cooperation, *http://www.berisoft.com/*) software package. In the beginning of each trial, an instruction indicating the type of task (complexity task or font task) was presented for 1 s on the screen. Afterwards, a daily life activity was displayed on the same screen. Within a fixed time of 3 s, participants had to make a decision on a hand-response pad with their right index (left button) or middle finger (right button). Stimulus presentation was event related and trials were separated by a randomly assigned jittered interstimulus interval of 4 s (range 2–6 s). For the complexity task, participants were asked to make a dichotomous decision regarding the complexity of daily life activities. In particular, participants were asked to rate each activity in terms of the number of events involved in the activity. Each activity may consist of few events (e.g. 'stirring a cup of coffee') or may consist of many events (e.g. 'planning a wedding'). Half of the participants were instructed to press the left button, if the activity has few events; or the right button, if the event has many events (and vice versa). In contrast, the font task participants had to decide whether the instruction word and the activity word were presented either in the same font or different fonts (Swiss or Helvetica Font). Half of the participants were instructed to press the left button if the same font was used and the right button otherwise (and vice versa). Participants were asked to make their decisions as quickly and accurately as possible while response times and decisions were recorded. After their responses, participants saw a blank screen for the rest of the trial. The fMRI experiment consisted of one 12-min run consisting trials from the control ($n = 33$) and experimental ($n = 66$) tasks. Stimuli were carefully matched for word length between the complexity and font tasks [$t(97) = 0.73$, $P = 0.467$].

Image acquisition

Imaging was performed on a 3 T GE MRI scanner (General Electric, Milwaukee, Wisconsin, USA) equipped with a standard circularly polarized head coil. Anatomical (T1-weighted 3D MP-RAGE sequence: repetition time = 9.7 ms; echo time = 4.0 ms; flip angle = 12°; field of view = 240 mm; matrix size = 256 × 256; thickness = 1.2 mm; in-plane resolution = $0.8594 \times 0.8594\,\text{mm}^2$) and functional images (T2*-weighted 2D gradient EPI sequence: repetition time = 2s; echo time = 30 ms; flip angle = 90°; thickness = 6 mm; number of slices = 22; field of view = 240 mm; in-plane resolution = $3.75 \times 3.75\,\text{mm}^2$) were acquired. For the functional runs, 401 volume images per run were taken parallel to the AC-PC line, and the first five volumes were discarded to allow for T1 equilibration effects. Participants had to lie flat on their back in the scanner and viewed the screen by a mirror system attached to the head coil. Stimuli (18-point font type) were back projected onto a translucent screen placed at the feet of the participant. Head motion was restricted using foam pads placed around the participants' head.

Image analysis

Image analyses were performed using BrainVoyager QX (Brain Innovation, *http://www.BrainVoyager.com*). The following data preprocessing steps were applied: slice scan time correction (using sinc interpolation), linear trend removal, temporal high-pass filtering to remove low-frequency nonlinear drifts of three or fewer cycles per time course, spatial smoothing (8 mm full-width at half-maximum), and three-dimensional motion correction to detect and correct for small head movements by spatial alignment of all participants to the first volume by rigid body transformation. Estimated translation and rotation parameters were inspected and never exceeded 2 mm or

2°. To transform the functional data into Talairach space [11], the functional time series data of each participant was first coregistered with the participant's three-dimensional anatomical data set and resampled to $3 \times 3 \times 3\,\text{mm}^3$ isotropic voxels.

A general linear model corrected for first-order serial correlation was applied. Random-effect analyses were performed on the multisubject level ($n = 18$) to explore brain regions that were associated with judgment of complexity. The regression model consisted of a set of four predictors. Besides one predictor for the instruction of the tasks (Instruction) and one for the font discrimination task (font), two additional predictors were created: one coding for the main modulation of the complexity evaluation task (main) and the other coding for the parametric modulation of the complexity evaluation task (parametric) for which the normative complexity ratings were applied.

Regressor time courses were adjusted for the hemodynamic response delay by convolution with a double-γ hemodynamic response function. Multiple regression analyses were performed independently for the time course of each individual voxel. After computing the coefficients (parameter estimates) for all regressors, *t*-tests were performed between coefficients of different conditions. A statistical model on the main modulation of complexity was fit for a linear contrast to explore brain regions that were associated with the complexity judgment task (main > font). Furthermore, a statistical model on parametric modulations of complexity was fit for a linear contrast to explore brain regions that differed in their activation according to complexity variation (main parametric). The conjunction of the two predictors provides the specificity about the coded linear parametric effect, requiring both a significant main effect and a significant modulation effect ('minimum *t*-statistic'). Activation was reported in a whole-brain analysis using an FDR with a threshold of q(FDR) less than 0.05 (corrected) [12]. For display purposes, statistical images were superimposed on a template structural brain in Talairach space and thresholded at P value less than 0.005, uncorrected ($t = 3.22$, random effects). Brodmann areas (BA) were determined by using the Talairach Daemon Client software (Research Imaging Center, *http://ric.uthscsa.edu/*).

Results

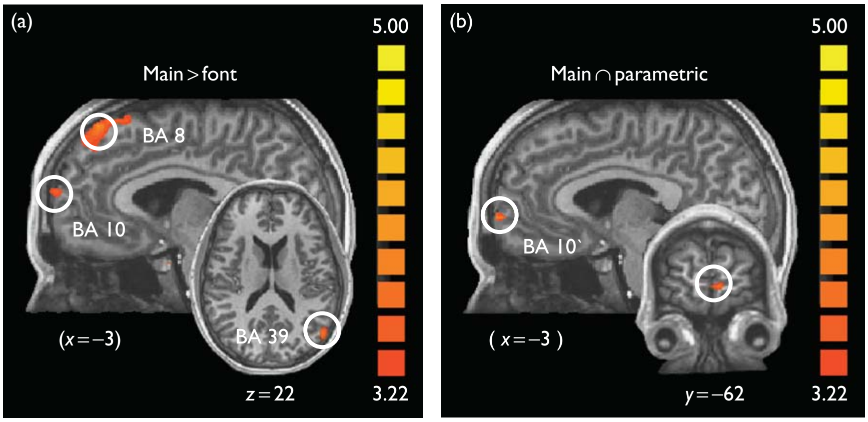
Behavioral data

The response times (mean ± SEM) for the font task (1304 ± 463 ms) were faster than for the complexity task (1504 ± 350 ms) [$t(17) = -3.60$, $P < 0.002$]. In addition, the response times for the complexity task increased with complexity ($r = 0.489$, $P < 0.001$), but was independent of the emotion ratings ($r = -0.044$, $P = 0.723$).

Imaging data

First, the control condition was contrasted with the experimental condition to identify brain regions mediating daily life activities independent of the modulation of complexity. The first contrast elicited activations in a left frontoparietal network including the medial frontopolar cortex [BA 10; *x,y,z*: −3,65,15; peak: $t(17) = 3.60$], dorsomedial PFC [BA 8; *x,y,z*: −3,40,55; peak: $t(17) = 3.11$], premotor cortex [BA 6; *x,y,z*: −25,22,57; peak: $t(17) = 4.59$], and posterior inferior parietal lobule [BA 39; *x,y,z*: −48,−76,25; peak: $t(17) = 5.32$] (Fig. 1a). Second, a parametric approach was used to test for a linear relationship between changes in complexity ratings

Fig. 1



Brain activation for event knowledge complexity. (a) The brain regions that were activated by the complexity judgment task included a left frontoparietal network: medial frontopolar cortex (FPC) [Brodmann areas (BA) 10], dorsomedial prefrontal cortex (BA 8), premotor cortex (BA 6), and posterior inferior parietal lobule (BA 39). (b) The parametric effect of complexity revealed a distinct activation in the medial FPC (BA 10), indicating that the higher the complexity of the activity was, the more activated was the FPC. Note that for display purposes statistical images were superimposed on a template structural brain in Talairach space and thresholded at $P < 0.005$, uncorrected ($t = 3.22$, random effects).

and changes in the blood oxygen level-dependent signals during processing of daily life activities. The second contrast revealed a distinct medial frontopolar cortex [BA 10; x,y,z: $-6,62,4$; peak: $t(17) = 3.97$] activation, indicating that the higher the complexity of the activity was, the higher was the activation in the medial frontopolar cortex (Fig. 1b).

Discussion

Event knowledge is sequentially and hierarchically organized on the basis of goals and represents the underlying cognitive architecture for carrying out plans, controlling a course of actions, or organizing daily life activities. We used parametric event-related fMRI to investigate brain activations when individuals evaluated the complexity of daily life activities. First, we identified a left frontoparietal network that is likely responsible for encoding and manipulating different aspects of event knowledge representations [13]. As the left hemisphere is more adept at constructing determinate, precise, and unambiguous representations of the world [14], it is designed to mediate the primary meaning of within-event information, sequential dependencies between single adjacent events, and coding of boundaries between events [15]. Second, within the frontoparietal network, we isolated the medial frontopolar cortex as the key region that showed a positive linear relationship between changes in the blood oxygen level-dependent signal and changes in the complexity of daily life activities.

According to our structural and temporal representation binding theory, the dorsomedial PFC represents abstract dynamic structured summary representations that give rise to event goal knowledge by binding with regions in the posterior cerebral cortex [8]. Association areas exist at multiple hierarchical levels ranging from posterior association areas to increasingly complex association areas in anterior brain regions. The dorsomedial PFC located at the apex of this hierarchy serves as a convergence zone [16] encompassing a multimodal representation distributed throughout the brain's association and modality-specific areas. We argue that by recognizing daily life activities, a subset of neurons in the dorsomedial PFC can partially reactivate event goal knowledge in the absence of bottom-up sensory stimulation, and inferences about this activity can be drawn by pattern completion. Functional neuroimaging studies have constantly shown the involvement of the dorsomedial PFC in mediating event goal knowledge [4,6,7,17]. In addition, there exists confirming evidence that damage to the dorsomedial PFC leads to an inability to set goals, devise plans, and comprehend the mental states of others [18].

Reenactment of event goal knowledge content arises through the dorsomedial PFC goal pathway through structural and temporal binding of distributed representations stored in spatially separate cortical areas in the posterior cortex [8]. This goal pathway has reciprocal connections with brain regions such as premotor cortex and posterior inferior lobule, which were also selected during the complexity judgment task [19]. The premotor cortex activation is consistent with findings of other neuroimaging studies dealing with motor preparation and sequencing of event knowledge [5,17]. Moreover, the posterior inferior parietal lobule has been shown to be engaged in mediating the time scale of event knowledge [3]. For example, a PET neuroimaging study focused on the temporal grain of event knowledge [4]. Long-term event order verification (e.g. 'growing a crop') was associated with activation in the posterior inferior parietal lobule (BA 39), whereas short-term event order verification (e.g. brushing one's teeth) was associated with stronger activation in the anterior inferior parietal lobule (BA 40).

Importantly, the medial frontopolar cortex (BA 10) was the only region in the frontoparietal network that became more activated as the complexity for daily life activities increased. The frontopolar cortex is probably the single largest cytoarchitectonic area of the PFC [20]. A recent meta-analysis [21] revealed a function variation within frontopolar cortex (BA 10) mirroring neurophysiological evidence for cytoarchitectonic differences between lateral and medial subregions of the PFC. Studies involving working memory and episodic memory retrieval were associated with lateral activations, whereas studies involving mentalizing (i.e. attending to one's own or others goal states) were associated with medial activations. The medial frontopolar cortex is among one of the last brain regions to mature and are, therefore, ideally suited for representing more general hierarchically organized event goal knowledge required for guiding behavior over progressively longer temporal intervals [22]. We suggest that participants estimated the complexity (i.e. number of events) of daily life goal activities by accessing the sequential and hierarchical structure of event goal knowledge. This enabled participants to simulate specific event sequences and, thus, gain a rapid estimate of the number of events required to accomplish the activity. Importantly, response time correlated with complexity ratings, supporting our view that participants judged the complexity of the activity by estimating the number of events required to complete the activity.

It could be argued that the observed medial frontopolar cortex activation is because of the increase in task difficulty rather than the specific proposed mechanism. However, there is evidence arguing that task difficulty is not sufficient to characterize frontopolar cortex activation. For example, neuroimaging studies in the working memory literature have shown that increasing the working memory load linearly did not lead to linear increases in frontopolar cortex activity but in dorsolateral PFC activity [23,24]. Furthermore, frontopolar activity activation was demonstrated with decreasing task difficulty. Although deductive reasoning is more difficult than inductive reasoning, the latter selected the frontopolar cortex whereas the former did not [25]. Those findings suggest that activation in the frontopolar cortex is not driven by increased difficulty *per se*, but that there are additional and qualitatively different mechanisms mediated by the medial frontopolar cortex compared with other brain regions.

In conclusion, our results further specify the role of the medial frontopolar cortex in subserving event knowledge that provides the underlying cognitive structure for the human ability to build and execute complex behaviors ranging from carrying out plans to organizing daily life routines.

Acknowledgements

The authors are grateful to Eric Wassermann for his help with performing the neurological exams. This research was supported by the Intramural Research Program of the NIH/NINDS/CNS.

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