Executive Function and Higher-Order Cognition: EEG Studies

L Y Deouell, The Hebrew University of Jerusalem, Jerusalem, Israel
R T Knight, University of California at Berkeley, Berkeley, CA, USA

© 2009 Elsevier Ltd. All rights reserved.

Introduction

Multiple goals, from survival to pleasure, coexist at every given moment, and internal needs as well as external events act in a push–pull manner to bias behavior. To maintain optimal goal-directed behavior, a control (‘executive’) system is needed that will dynamically prioritize the processing of information as well as the planning of actions and their execution. In addition to direct motor planning, major components of this executive system are working memory, attention, and conflict/error monitoring. Working memory would allow maintaining a goal across time, as well as information required to achieve the goal. Selective attention (‘voluntary’ or ‘endogenous’ attention) would facilitate the processing of one stream of input and suppress another while involuntary attention mechanisms allow for changes in the environment, as well as changes in internal drives, to interfere with ongoing behavior in a rapid and flexible manner. A monitoring module is needed to assess the efficiency of the executed behavior so that behavior can be adjusted in an optimal way. Consequently, the executive system needs to interact with multiple sensory regions of the brain, as well as with motor output regions involved in orientation, locomotion, and speech. Event-related brain potentials (ERPs), recorded on the scalp (and recently also intracranially) have established scalp-recorded signatures of executive functions. The effect of brain lesions on these measures of electrical brain activity provides a window into the networks supporting the executive system. This article describes ERP studies conducted specifically with patients suffering from well-circumscribed brain lesions involving mainly the lateral prefrontal cortex (LPFC), a major hub of the executive system.

Selective Attention

Patients with LPFC damage are frequently unable to suppress inappropriate reaction to objects and events in their environment (so-called environmental dependency syndrome) or to suppress prepotent responses. Whereas some of these effects may be at the level of response selection, ERP studies of these patients suggest that LPFC is essential for normal suppression of information processing at the level of unimodal sensory cortices.

Knight and coworkers delivered auditory stimuli (clicks or tone bursts), or brief electric shocks to the median nerve, to patients with damage to LPFC and to patients with comparably sized lesions in the temporoparietal junction or the lateral parietal cortex, as well as to age-matched controls. Both types of stimuli were distractors, not relevant to the task. Lesions in posterior association cortex, sparing primary sensory regions, had no effects on the amplitudes or latencies of the primary cortical evoked responses. Lesions invading either the primary auditory or somatosensory cortex reduced early latency (20–40 ms) evoked responses generated in these regions. In a distinct contrast, LPFC damage resulted in enhanced amplitude of both the primary auditory and somatosensory evoked responses generated 20–40 ms poststimulation. Spinal cord and brain stem potentials were unaffected by prefrontal damage, indicating that the amplitude enhancement of primary cortical responses was due to abnormalities in either prefrontal-thalamic connectivity or direct interactions between LPFC and sensory cortex. Selectively attending to a sensory stream and maintaining the goal of behavior requires not only enhancement of processing of some sensory stimuli or motor plans, but also suppression, or inhibition, of competitive stimuli or plans (‘biased competition’). Apparently, a signal from LPFC to upstream sensory cortices provides such a biasing signal. Failure to produce such a signal may impair selective attention.

The failure to inhibit irrelevant sensory input indeed affects the patients’ performance. Chao and Knight showed that patients with LPFC lesions are impaired in an auditory delayed-match-to-sample task when the delay period is filled with irrelevant tone pips. In the same task, the irrelevant tones elicited abnormally augmented primary auditory potentials (Na, Pa) in the patients, and the performance decrement directly correlated with the Pa enhancement. Similarly, in patients with right prefrontal damage, sounds presented to an unattended ear in a dichotic paradigm abnormally reduced the attentional enhancement (see the section titled ‘Novelty and deviance detection and involuntary attention shift’) of subsequent to-be-attended sounds. In agreement with these findings, patients with prefrontal lesions show reduced or even reversed negative priming effects, which suggests that processing of stimuli that should be outside the focus of attention is not properly suppressed.

The role of the LPFC in biased competition is not limited to inhibition. In fact, LPFC may also provide the excitatory signal. This excitation may be
implemented through three distinct mechanisms: (1) through a tonic excitatory influence on ipsilateral posterior areas, affecting attended and nonattended sensory inputs alike; (2) by enhancement of extrastriate cortex response to attended information; and (3) by a phasic excitatory influence on ipsilateral posterior areas’ response to correctly perceived task-relevant stimuli (targets). This was shown in a series of ERP studies conducted by Knight and colleagues in patients with LPFC damage (centered on Brodmann’s areas 9 and 46), in which the patients were asked to detect rare (odd ball) targets (inverted triangles) in a series of distractors (upright triangles). This paradigm is referred to below as the triangles task.

When the stimuli in the triangles task were presented at fixation, the patients showed a diminished extrastriate N1 component (at 170 ms) relative to controls. A similar reduction of N1 was observed in another experiment, which used visual word stimuli. Even more revealing were conditions in which targets and nontargets were lateralized and could appear in either visual field. In one of these conditions, the patients were instructed to attend to all stimuli regardless of location. The extrastriate P1, immediately preceding the N1 component, was reduced for all stimuli presented to the contralesional hemifield. Moreover, when the patients’ attention was directed to one of the fields at a time, this reduction of P1 over ipsilesional extrastriate cortex was observed for attended and nonattended contralateral stimuli alike, and can thus be considered attention independent. Thus, LPC seems to exert a modulatory, tonic, attention-independent facilitation over processing at ipsilateral extrastriate cortex. A similar effect of reduced association cortex activity ipsilateral to LPFC damage has been reported for auditory-induced N1 potentials.

Directing attention to one hemifield in a target detection task normally elicits a sustained negativity (known as ‘selection negativity’ or ‘negative difference’), starting at around 100 ms, for all stimuli presented at this hemifield. When attention was directed to the contralesional visual field of LPFC patients, this attention effect on extrastriate cortex was normal in the first 200 ms after stimulus onset but was significantly disrupted thereafter. This finding suggests that LPFC exerts attention-dependent selective facilitation starting around 200 ms after stimulus onset. Other cortical areas are probably responsible for attention-dependent regulation of extrastriate cortex in the first 200 ms. It is conceivable that inferior parietal cortex is responsible for the early reflexive component of attention whereas LPFC is responsible for more-controlled and sustained aspects of visual attention beginning later on. The effect of LPFC lesion on the selection negativity is not limited to visual areas. In an auditory selective attention task, prefrontal lesion patients generated reduced selection negativity as well. Notably, this diminished attention effect depended on the side of the lesion. Patients with left hemisphere lesions showed a mildly reduced attention effect regardless of which ear was attended. In contrast, patients with right prefrontal damage showed reduced effect mainly when the contralateral ear was to be attended. Posterior association cortex lesions in the temporoparietal junction had comparable effects on the selection negativity regardless of ear of stimulation.

Target detection in the visual oddball paradigm described above is normally associated with a prominent late response, starting at 200 ms and continuing for the next 500 ms, including the N2–P3b complex. Since this component is elicited only by detected targets, it is considered to be a manifestation of phasic top-down effects contingent on the identity of the stimulus. Following LPFC lesions, the N2, a component which likely reflects postselection processing of the target in the inferior temporal lobe, was not observable over the lesioned hemisphere in response to targets in either visual field. The P3b was reduced over the temporocortical electrodes but not at parietal sites, attesting to the fact that the P3b most likely reflects multiple distinct cortical processes related to target detection. The patients’ performance in this study, producing more errors, was concordant with this electrophysiological evidence of impaired top-down effects following LPFC lesion. A spatially limited reduction of target P3 was recently reported also by Daffner et al., although in that group of LPFC patients, the main reduction of target P3 was reported to be in anterior electrodes. Thus, in addition to both attention-dependent and attention-independent tonic facilitation, the LPFC is critical in establishing a phasic, stimulus-dependent facilitation.

**Novelty and Deviance Detection and Involuntary Attention Shift**

Task requirements in an experimental setting, as well as the ongoing goals in natural settings, require that a subset of the sensory stream and a subset of motor plans be preferentially processed and, at least in humans, be available for conscious awareness and deliberation. However, such biased selection may be perilous as events outside the focus of attention might pose either dangers (e.g., an approaching predator) or opportunities (e.g., prey). Such events may be slight perturbations of an established sensory regularity, such as an intensity decrement in background noise, or grossly unexpected (‘novel’) events, such as the sound of screeching brakes. This need calls for a
surveillance mechanism that automatically detects deviant events.

Automatic response to slight changes in acoustic regularity outside the focus of attention bears the electrophysiological signature of the ‘mismatch negativity’ (MMN), a frontal scalp negative potential accompanied by lower temporal positivity, with a peak latency of 100–250 ms following the deviation. The MMN presumably reflects an ‘error signal’ generated automatically in the secondary auditory cortex by a neural mechanism comparing a perceived stimulus to a sensory ‘memory trace’ formed by the regular stimuli or the process of updating the existing model of the environment. The MMN is elicited when participants attend to a primary task and ignore the stream of sounds in which the pertinent deviations occur. Although it might be somewhat attenuated outside the focus of attention, it is completely suppressed only under very specific circumstances of competition for processing a specific feature between two auditory streams. Moreover, whereas attention-related components of the ERP are largely absent when deviation is predictable (e.g., when a deviation occurs regularly in the stream), the MMN is immune to this manipulation. Thus, the MMN is considered to represent a nonintentional, largely preattentive process. This signal may be a trigger for an ensuing shift of attention toward the deviant event. These shifts are reflected on the scalp as a positivity following the MMN, called P3a.

The P3a is a positive frontoparietal scalp potential peaking around 300 ms following the onset of a rare, task-irrelevant distractor in an oddball sequence. The novelty P3a is similar in response to either novel sounds or visual stimuli. The P3a is considered a marker of attention orienting, elicited by a distributed multimodal corticolimbic system. Both the MMN and the novelty P3a components were shown to be reduced in patients with PFC lesions.

In paradigms designed to study the MMN, patients and controls watched silent movies or were engaged with a visual reaction time paradigm and were instructed to ignore series of repetitive sounds. Infrequently, the regularity of the sound stream was broken by the occurrence of a deviant stimulus. The MMN in response to pitch and pattern changes was reduced in patients with PFC lesions, indicating an early deficit in automatic detection of deviance outside the focus of attention. Whereas temporoparietal lesions caused an MMN reduction mainly to contralosional stimuli, LPFC lesions elicited comparable deficits regardless of stimulus side in one study, and more to ipsilesional sounds in another. In addition, there was a tendency for right prefrontal lesions to be associated with larger MMN reductions than left prefrontal lesions were, but no such asymmetry was found for the temporoparietal lesions. These results suggest different contributions of the temporoparietal region and the prefrontal region to the MMN. Further research will be needed to determine whether the reduced MMN following prefrontal damage reflects a weakened memory trace of the previous regularity due to disinhibition of irrelevant information, reduced frontal facilitation of a comparator mechanism in the secondary auditory cortex (which is the main generator of scalp MMN), or a failure to initiate an attention switch following the detection of the change, or damage to a postulated frontal generator of MMN. In addition, it is still unclear whether the effect of LPFC damage is independent of the dimension of the regularity which is disturbed (e.g., spatial location, pitch, or more-abstract dimensions of the sound).

Novelty P3a responses generated over prefrontal scalp sites to unexpected novel stimuli are reduced by prefrontal lesions, with reductions observed throughout the lesioned hemisphere. Comparable P3a decrements have been observed in the auditory, visual, and somatosensory modalities in humans with prefrontal damage. Reductions appear to be more severe after right prefrontal damage. In most studies of novelty P3a, the novel stimuli are completely task irrelevant, and the response is considered to reflect an ‘involuntary’ orienting response toward the salient event. Accordingly, galvanic skin response, a peripheral marker of the orienting response, is also reduced by damage to the prefrontal as well as posterior association cortex. LPFC damage caused a dramatic reduction in P3a amplitude even in a paradigm in which the novels where relevant to one of two tasks the patients were involved with. In the paradigm used by Daffner et al., patients had to self-pace a succession of visual stimuli while also looking for a designated (non-novel) target. LPFC patients not only showed a significantly attenuated P3a response to novel visual stimuli but also spent less time than controls did looking at novels, suggesting a more general decrement of ‘novelty seeking.’ Taken together, these findings converge with both clinical observations and animal experimentation supporting a critical role of prefrontal structures in the processing of novel stimuli, probably as part of a prefrontal-hippocampal network.

**Monitoring**

In demanding task situations, it is important to detect when actions may be erroneous and to adjust behavior to avoid additional mistakes. Evidence from electrophysiological and neuroimaging studies suggests that the anterior cingulate cortex (ACC) and the LPFC are active in situations demanding such monitoring activity. Evidence linking the ACC to action monitoring...
derives from studies of error-related negativity (ERN), an ERP that occurs at the moment of an error in cognitive reaction time tasks. Dipole localization studies of ERN suggest that it is generated by a medial frontal structure, most likely the ACC. Functional magnetic resonance imaging (fMRI) studies examining error processing confirm the presence of ACC activation associated with errors or with situations prone to errors. A rare single unit recording in a human patient showed that dorsal ACC is associated with the use of rewards to guide action and further that ablation of the dorsal ACC increases errors in a situation requiring reward processing. Also, fMRI studies demonstrate that in addition to the ACC, activation may occur also in LPFC in conflict situations. Some of these studies suggest that activation in the ACC and LPFC is not related to errors per se but rather to the need to avoid errors or losses in more-demanding situations. Co-occurrence of prefrontal and cingulate activity related to error processing has been observed also in single-neuron recordings from nonhuman primates, as well as in intracerebral recordings from implanted depth electrodes in epileptic patients. These observations have not determined, however, whether the ACC and the LPFC interact or are independent.

The question of the interaction of the ACC and the LPFC was investigated by Gehring and Knight, who measured ERN in a group of patients with unilateral circumscribed lesions of the LPFC. A normal pattern of ERN activity in these individuals would indicate that the medial frontal regions operated independently of the LPFC in generating the ERN. In contrast, an absence or reduction of ERN activity in these individuals would indicate that the LPFC was either necessary for generation of the ERN in the ACC, or was itself a generator of the ERN. Other disruptions in the pattern of ERN activity would suggest that LPFC modulated the generation of the ERN, perhaps by supplying information or activation that was critical for ACC processing.

Six patients were studied, four with left and two with right LPFC damage. They were compared to ten age-matched controls and ten younger individuals. Participants made a squeezing response to a pair of letters, one of which was designated as a target letter. One letter appeared in red and the other in green. At 1 s before the letter pair, a precue (the word ‘red’ or ‘green’) indicated which letter was the target letter. The task was to respond with one hand if the target letter was ‘H’ and with the other hand if the letter was ‘S’. On half of the trials, the irrelevant flanking letter was identical to the target letter; on the other half of the trials, the irrelevant flanking letter signaled the incorrect response (a manipulation that provoked erroneous responses).

The patients were slower than the control groups but did not perform with more errors than the control groups did. However, they showed less online corrective action in error trials. While controls showed reduced squeezing force during error trials, suggesting online inhibition of response, patients showed a reduction in this effect. In addition, the patients corrected their error less frequently than controls did. The pattern of the patients’ electrophysiological response was also dramatically different from that of the control groups. Whereas in the young and age-matched controls, the response-locked negativity was significantly larger during error trials than during correct trials (i.e., it was an ERN), there was no difference between the error and correct trials in the patients with LPFC lesions. However, this did not result from absence of negativity. Rather, an ERN was seen for correct trials just as often as for incorrect trials, and this ERN was not different in amplitude from the response elicited by the controls during incorrect trials.

This pattern suggests an interaction or interdependence between the LPFC and the ACC in error or conflict monitoring. However, it is not consistent with a simple serial model in which the LPFC detects the need for executive control during high-conflict situations and signals the ACC, which performs the actual control function. Nor is it compatible with a serial model in which the ACC detects conflicts and transmits to the LPFC, which exerts its executive control functions. Since the most conspicuous observation was the lack of differentiation between correct and error trials, one possible account suggested by Gehring and Knight was that the damaged LPFC failed to represent or transmit the contextually appropriate stimulus–response mapping. As a consequence, the ACC may not have been able to confirm a correct response and thus elicited an ERN by default for every trial. Alternatively, the impaired stimulus–response representation in the LPFC might have created an additional conflict in each trial, detected by the ACC. In both cases, the ACC would produce an unreliable cue for errors, reflected in the disruption of corrective responses.

**Conclusion**

The behavior of patients with LPFC lesions suggests an interruption of executive and attentional control at multiple levels. Thus, in everyday life, patients may inadequately respond to environmental stimuli, be disproportionately distracted by irrelevant information, and be unable to focus on a task, on the one
hand, and unable to flexibly shift from one goal to another (perseveration), on the other hand. The data from electrophysiology reveal the role of LPFC in automatic processes such as maintaining an adequate level of responsiveness to all stimuli, detecting change, and processing novelty, as well as controlled processes such as inhibition of irrelevant information, enhanced processing of relevant information, phasic responses to targets, and conflict monitoring. Moreover, the electrophysiological data reveal that LPFC implements some of these functions through interaction with remote regions of the brain, including unimodal sensory cortices, the hippocampus, and the ACC. All these effects are evident early (100–300 ms) in the course of neural processing.

See also: Attention: Models; Attentional Functions in Learning and Memory; Cognitive Control and Development; Electroencephalography (EEG); Electrophysiology: EEG and ERP Analysis; Executive Function and Higher-Order Cognition: Assessment in Animals; Executive Function and Higher-Order Cognition: Definition and Neural Substrates; Working Memory: Capacity Limitations.

Further Reading