1. INTRODUCTION

In the past few decades one of the most important questions in understanding higher order cognitions concerned the nature of the executive function and its neural implementation.

Executive functions represent the farthest reaches of human nature. Whereas many neuropsychological functions are shared with other mammalian species, homo sapiens appears unique in using the mental tools that allow consciousness and the dynamic shaping of environments. The neurological substrate for this executive regulation of complex cognition and social behavior is strongly, but not exclusively, that of the frontal lobes (Callahan & Hinkebein, 1999; Kolb & Bryan, 2007).

The dramatic expansion of the human frontal lobe (particularly the prefrontal structures), now accounting for nearly 30% of the cortical surface area, is a recent evolutionary event. Similarly, at the level of the individual, the chronologically-delayed development of the frontal lobe mediated executive functions is synonymous with the demarcated signs of competent adulthood: the ability to anticipate, understand, and to be held accountable for the consequences of one's actions. Today, the prefrontal cortex is considered as the seat of a high-level system (or systems) that receives input from more specific lower-level systems and than in turn, modulates or controls their operations (e.g. Shallice, 1988, 2002; Goldman-Rakic, 1987; Miller & Cohen, 2001). The prefrontal cortex is highly complex, with major functional differences between the lateral, orbital and medial surfaces, along with increasing levels of abstraction of its functions as one moves toward the frontal pole. The functioning of these regions has been viewed within a number of different conceptual frameworks. This introductory section provides an overview of these various frameworks, puts forward the resarch questions and introduces some of studies to be presented in the next sections.

1.1. Theoretical frameworks

A link between executive funtions and the frontal cortex has been strongly suggested in human neuropsychology by classic authors, such as Luria (1966), Milner (1964), Harlow (1868) and more recently by authors such as Shallice (1988, 2002) and Shimamura (1995). In one of the first modern attempts to describe the functions of the frontal cortex, Luria (1966) suggested that the frontal lobes contain a system for the programming, regulation, and verification of activity. This view was more in keeping with the ideas and methods of cognitive neuroscience than most previous accounts, and formed the basis of many subsequent cognitive models of frontal functioning (e.g. Shallice, 1988; Miller & Cohen, 2001). However, although rich and insightful, Luria's understanding of frontal functions was biased by several factors. First, the bulk of his reports consisted only of clinical observations, and was rarely compared to control participants, or to patients with other kinds of neuropsychological problems. Second, given that no CT or MRI scans were available at the time, the level of control for lesion location was limited. Consequently, very often patients presented massive lesions extending outside the frontal lobes. Conversely, patients with lesions involving only frontal structures had little or no difficulty with Luria's problem solving tasks (Canavan et al., 1985; Andres, 2003; Andres & Van der Linden, 2004).

The most influential neuropsychological model suggesting a specific link between frontal lobe and executive functions (Shallice, 1988; 2002) was strongly inspired by Luria's view and the attentional model of Norman and Shallice (1980). This model differentiates two types of control-to-action mechanisms. The first type involves the Contention Scheduling (CS), a system involved in routine situations in wich actions are automatically triggered. The second type involves the Supervisory Attentional System (SAS), a separate system at the high level of action control that allows to cope with novelty, required in situations where routine selections of actions are unsatisfactory and where generation of novel plans and willed actions are needed (Shallice, 1988; Shallice & Burgess, 1991, 1993; Burgess & Shallice, 1996; Burgess et al., 2000; Shallice, 2002). Shallice introduced his hypothesis as „an attempt to anchor the overall theory that Luria applied to 'frontal functions' within a cognitive science conceptual framework" (Shallice, 1988, p.332). The core idea was that the cognitive impairments observed in patients with frontal lesions could be attributed to a deficit of the SAS. Clearly, Shallice was establishing the hypothesis of a one-to-one relationship between the frontal lobe and the executive functions and this remains in fact the dominant view among clinical neuropsychologists.

The original working memory (WM) model of Baddeley (Baddeley & Hitch, 1974; Baddeley, 1986; Baddeley & Della Sala, 1996) similarly suggests a specific link between the central executive of working memory and the frontal lobe. The model proposed by Baddeley (1986) includes two slave systems enduring temporary storage of information, the phonological loop and the visuospatial system, and an attentional system, the central executive (CE). The CE is by far the most complex component of working memory, and Baddeley suggested that it could essentially be understood as an equivalent to the Supervisory Attentional System (SAS) described by Norman and Shallice (1980). Baddeley in 2000 revised his original WM model, and proposed a fourth component to the model, the episodic buffer. This component comprises a limited capacity system that provides temporary storage of information held in a multimodal code, which is capable of binding information from the subsidiary systems, and from long-term memory, into an unitary episodic representation by integrating information from a variety of sources. It is assumed to be controlled by the CE, which is capable of retrieving information from the store in the form of conscious awareness, of reflecting on that information and, where necessary, manipulating and modifying it. The revised model differs from the old principally in focussing attention on the processes of integrating information, rather than on the isolation of the subsystems. In doing so, it provides a better basis for tackling the more complex aspects of executive control in working memory.

From a neuropsychological perspective, it has been recently pointed out that little is known about the neural substrate of the CE. The hypothetical link between CE and frontal lobe was originally suggested by Baddeley (1986) following the analogy between CE and SAS. However, Baddeley has on several occasions recommended dissociating the concept of executive functions from their neural substrate, particularly from their frontal location and the performance of patients with frontal lesions (Baddeley, 1996, 1998a, 1998b; Baddeley & Wilson, 1988; Baddeley & Della Sala, 1996). Baddeley and Wilson (1988) suggested the term of 'dysexecutive syndrome' to allow the discussion of functions to be separated from the question of the anatomical locations of such functions. Baddeley emphasized also that the CE is fractionable, and that its functions are independent from each other (Baddeley, 1998a, 1998b). Importantly, Baddeley (1996) made a clear distinction between inhibition (the ability to select relevant information while rejecting the irrelevant information) and co-ordination of two or more concurrent activities in working memory.

1.2. Inhibition as a main component of the executive system

Inhibition was early emphasized also by Norman and Shallice (1980) as one of the main SAS or executive functions and it has been probably the most extensively explored one in neuropsychological studies. The term inhibition can be used in many different ways, but in general it is defined as a mechanism that reduces or dampens neuronal, mental, or behavioral activity. The contribution of inhibitory processes to cognitive control and executive functions has received increased interest during the last few decades. In classical neuropsychological cases, a deficit of inhibition has been described in frontal lobe patients since the famous case of Phineas

Gage (Harlow, 1868; Milner, 1964; Damasio, 1996; see Stuss, 1991, for review). Lurija (1966, 1975, 1976) also decribed particular signs of disinhibition (perseverations, stereotypes, behavioural disinhibition, etc.) in patients with large frontal lobe lesions. Overall, neuropsychological researchers have suggested that the deficit of inhibitory mechanisms is scpecifically associated with frontal lobe lesions (e.g. Dempster, 1995; Shallice, 1988; Shimamura, 1995; Conway & Fthenaki, 2003; see however Andres, 2003, 2004 for critique), but it still remains a debated question which specific brain regions are responsible for distinct inhibitory functions. *This question is investigated in detail using lesion studies in Section 2.1-Section 2.4, with the help of four widely used experimental procedures, testing for automatic /intentional attentional and memory inhibitory processes.*

The automatic and intentional inhibitions play an important role in executive processes and emotions may interfere with the effectiveness of the executive system. The relationship between cognitive processes and emotions have occupied an important place in the study of human behavior for a long time, being also the subject of extensive investigation in psychopathology, as cognitive processes are thought to play a role in symptom production and maintenance, particulary in affective disorders (Rapaport, 1971). On the other hand emotions also influence cognitive processes, and affective disorders provide an especially good opportunity to examine the way in which cognition is influenced by emotion (Kulas, Conger, Smolin, 2003). Emotions are functional because they signal events which are important for the organism and also prepare the body and mind to react to them (Tobby & Cosmides, 1990; Payne & Corrigan, 2006). For example emotions draw attention to the most relevant aspect of the environment, they are signals that an event is important and requires a response, and also guide decision-making (Murphy & Zajonc, 1993; Damasio, 1996; Roberts & Wallis, 2000; Bechara, Damasio & Damasio, 2000). From an adaptationist perspective a well designed cognitive system is likely to build in a preference for emotional signals.

In a well-known study based on this rationale, Brown and Kulik (1977) predicted that dramatic events such as the assassination of John F. Kennedy should produce strong and detailed photograph-like memories. Although such “flashbulb” memories do appear to be accompanied by subjective qualities such as vividness and confidence, later research showed that they are not necessarily accurate (Neisser & Harsch, 1992). In some cases, autobiographical memory for emotional events is more distorted than memory for neutral events. The perspective emerging from recent research puts these two views in a larger context. Even though emotional memories are not photograph-like copies of experience, well-controlled studies have shown that emotion can enhance memory accuracy (Ochsner& Schacter, 2000). Memory is strengthened most for the central, emotionally meaningful aspects of events, often at the expense of peripheral details (Easterbrook, 1959). Neuropsychological evidence suggests that interactions between the amygdala and hippocampus are critical (e.g. Ochsner & Schacter, 2000; McGaugh, 2003; Phelps, 2004). The amygdala is believed to alter how the hippocampus consolidates memories, resulting in preferential memory for emotional events. These findings suggest that, all else equal, emotional events are more likely to be remembered than unemotional events. We know almost nothing, however, about how emotional memories respond when people deliberately endeavor to erase them. This is an important question, because the effectiveness of a cognitive system depends not only from the maintenance and organization of relevant informations, but also on succesfull inhibition of irrelevant information. Negative emotions, like anxiety can have negative effect by disturbing the effectiveness of the executive system, causing pseudoexecutive symptoms even in people without organic defficits, or can alter non-executive neurological symptoms in brain injuried persons. Persons who suffered a brain-injury have to deal with negative emotions, especially anxiety, and this can alter the clinical syndrome. From differential diagnostic perspective it is especially important to be able to separate somehow the real dysexecutive symptoms from pseudo-executive symptoms caused by negative emotions. *Thus, the purpose of Section 2.5 and Section 2.6 was to investigate the effects of anxiety related emotions on executive processes by using emotional inhibition paradigms with persons with generalized anxiety disorder (GAD) and to compare their performance with frontal lobe injured patients' performance.*

1.3. The role of lateralized executive functions in memory retrieval

Despite the enormous number of studies, the concept of executive function remains elusive. However, the common characteristic of old and new executive models is that the postulated executive subprocesses are considered to be domain general in the sense that they play an important role in a broad range of distinct cognitive domains (e.g., attention, working memory, episodic long-term memory) (Baddeley, 1996; Marklund et al., 2007). Memory is a constructive process that depends on strategic, controlled processes intermixed with more automatic processes to build a perception that is experienced as an incident from the past (Schachter, Norman, & Koutsaal, 1998; Buckner & Schacter, 2002). Multiple, interdependent processes support retrieval through interacting brain networks. Medialtemporal/ diencephalic structures are perhaps the best-understood contributors to memory. Areas within the medial temporal lobe appear to support memory processes that bind and/or associate new information. An additional broad class of processes that contribute to retrieval is required when sought-after information cannot be automatically accessed, and strategic processes must be engaged (Moscovitch, 1989; Buckner & Schacter, 2002). These controlled processes involve attention-demanding operations that are sequential in nature, are sensitive to capacity limitations, and are influenced by retrieval context. Not all retrieval tasks require strategic processes. In some situations, retrieval cues can automatically result in a perception that information is from the past, suggesting that certain retrieval processes can ocur spontaneously and are not dependent on strategic operations. Models of performance on recognition tasks have, in particular, long proposed distinctions that capture these separate retrieval processes (Jacoby, 1991).

Patients with frontal lobe lesions show impairment when retrieval requires controlled acces to past information. Difficulties are greatest when retrieval cues are minimal or when weakly associated information must be retrieved (e.g., during source retrieval). Patients tend not to show organized retrieval grouping typical of healthy young adults (Gershberg & Shimamura, 1995), and sometimes can exhibit excessively high false alarm rates (Buckner & Schacter, 2002) or even confabulation (Moscovitch, 1989). To summarize, in the memory domain, the executive processes are particularly involved in working memory, metamemory, generation of memory cues, monitoring contextual features like temporal order, strategic memory retrieval and memory inhibition (reviewed by Shimamura, 1995).

Recently, functional neuroimaging studies have associated remembering past events with increased neural activity in several brain areas, including prefrontal, medial temporal, posterior midline and parietal regions (reviewed by Cabeza & Nyberg, 1997; Nyberg et al., 2000; Mayes & Montaldi, 2001), but there is little evidence concerning the specific contributions of these regions to different aspects of episodic memory, mainly due to the methodological difficulties of differentiating between the various aspects and processes of episodic memory in a typical episodic memory test, such as free recall or item recognition. One way to delineate the neural correlates of different component processes underlying episodic memory is to compare performances across various tests specifically designed to emphasize different processes of episodic remembering.

Another major question concerning the neural basis of episodic memory is the separate roles of the two hemispheres in executive processes and episodic memory retrieval. In keeping with the general complementary organization of the left and right hemispheres, as a rule the left frontal lobe has a preferential role in language-related movements, including speech, whereas the right frontal lobe plays a greater role in nonverbal movements such as facial expression. Shallice (2002) in his model considered also the contrasting functions of left and right dorsolateral prefrontal cortex, emphasising that the left is held to be involved in top-down strategic modulation of lower-level systems while the right is considered to be more concerned with the control of checking that on-going behavior accords with task goal.

Lesion and fMRI data (Goel & Grafman, 2000; Paulus et al., 2001) point to the structural differences in the capacity of left and right PFC for encoding and manipulating certain types of representations. In particular, the left PFC is more adept at constructing determinate, precise and unambigous representations of the world, whereas the right PFC is more adept at constructing and maintaining fluid, indeterminate, vague and ambigous representations of the world (Goel et al., 2007).

Despite some observed laterality differences, it must be emphasised that, like the asymmetry of parietal and temporal lobes, the asymmetry of frontal lobe function is relative rather than absolute; the results of studies of patients with frontal lesions indicate that both frontal lobes play a role in nearly all behaviors. Thus, the laterality of function disturbed by frontal-lobe lesions is far less striking than that observed from lesions in the more posterior lobes. Nonetheless, as with the temporal lobe, there is reason to believe that some effects of bifrontal lesions cannot be duplicated by lesions of either hemisphere alone. However, there are a few theoretical models emphasising the separate role of the two hemispheres in the episodic memory.

The left-right contrast is emphasised in the well known Hemisphere Encoding and Retrieval Asymmetry model of Tulving, Kapur, and Craik (1994) proposing, that left PFC have a greater role in encoding information into memory, whereas the right PFC is more engaged than the left in retrieval. Recently developed new hypotheses, like the “cortical asymmetry of reflective activity” (CARA) model and the “production-monitoring” hypothesis propose alternative explanations for hemispheric dissociation. The CARA model states that the left PFC is more involved in systematic retrieval, while the right PFC is more active in heuristic retrieval (Nolde, Johnson, & Raye, 1998b). The “production- monitoring” hypothesis proposes that the left PFC is primarily involved in semantically guided production of information, while the right PFC is more active during monitoring processes (Cabeza, Locantore, & Anderson, 2003).

Thus, the main purpose of Section 3 was to present the role of the two hemispheres in the different executive processes during episodic memory retrieval using verbal and visual episodic memory tasks with patients with left- or right sided frontal or temporal lobe lesions.

1. 4. Common components of the executive functions

The classic neuropsychological approach has been an attempt to use lesion data, mapping the location of the lesion onto the nature of the deficit (Milner, 1964; Baddeley & Della Sala, 1998). While this has certainly had some success, the approach is limited by the lack of any obvious coherent pattern in the tasks impaired by frontal damage, which range from concept formation and verbal fluency through the capacity for making cognitive approximations to judgments of recency and the performance of various complex learning tasks. Attempts to look for meaningful clusters of tasks within this array using factor analytic techniques have in general proved to be disappointing: the various tasks tend to correlate modestly but significantly, without falling in any very clear pattern (Della Sala et al, 1996). Furthermore, none of the classic 'frontal' tests seem to capture the frequent gross behavioural derangments that typify patients with frontal lobe damage (Harlow, 1868). This is due to the fact that executive processes involve links between different brain areas, not exclusively with the frontal cortex, thus it is unlikely to be unitary in function (see Andres, 2003, 2004 for review). These difficulties stem in part, at least, from the failure of cognitive psychology to provide an adequate characterization of the executive processes. Recent models have suggested a view of the executive functions as a conglomerate of largely independent, but interacting control processes such as interference resolution, attention-shifting, updating, and inhibition (Johnson, 1992; Baddeley, 1996; Fuster, 1997; Smith & Jonides, 1999; Miyake et al., 2000; Friedman & Miyake, 2004; Marklund et al., 2007).

To refine frontal lobe brain-behavior relations, we tried to simoultaneously improve our differentiation of executive processes. In our lesion studies a greater number of patients were used to develop different approaches to localize distinct executive functions within the frontal lobes. We decided that it would be necessary to test as many patients as possible who might have lesions involving, and restricted to, any region of the frontal lobes. Although patients would have pathology that affected different frontal lobe areas, it was hypothesized that, if a particular region was relevant to a specific function, those individuals who had involvement in that distinct area would be impaired in that specific function, regardless of brain damage in other surrounding areas. Simoultaneously we moved from a comparison of frontal versus posterior lesions to what we called the standard anatomical classification within the frontal lobes: right frontal, left frontal, and bifrontal.

Thus, in Section 4 we aimed to examine the relation between the different executive components and episodic memory functions, trying to find common executive components in classic neuropsychological tests and in newly developed, experimental memory and executive tasks.

Finaly, Section 5 summarizes the experimental and clinical results, emphasising the different and separate roles of the two hemispheres and tries to provide an explanatory-integrative model of executive functions involved in episodic memory retrieval.

2. DISRUPTION OF INHIBITORY CONTROL

Control of behavior and impulse is a higher-order function that evolves late, phylogenetically as well as ontogenetically, and has been previously suggested to be subserved by the frontal lobes (Fuster, 1989; Dempster, 1995). Every behavioral, cognitive, or motor act requires a finely tuned balance between initiatory and inhibitory processes to provide appropriate preparation, initiation, on-line control, and timely inhibition of this act. Inhibitory control is therefore an essential regulatory function. It develops progressively from childhood to adulthood and is therefore susceptible to impairment in neurodevelopmental disorders such as attention deficit hyperactivity disorder, conduct disorder, antisocial personality disorder, obsessive compulsive disorder, and Tourette's syndrome (Rubia et al., 1999, 2001; Aron, Robbins, & Poldrack, 2004)

Different types of motor acts are likely to be regulated by different inhibitory processes, which may be mediated by different cortical areas. The parts of the frontal lobes specifically involved in inhibitory control may therefore depend on the type of the inhibitory process and the kind of action which needs to be inhibited. Concordant with this multiple domain model, different parts of the frontal lobes have been found to be responsible for different aspects of inhibitory control. Lesions in orbitofrontal cortex can lead to behavioural and socio-emotional dyscontrol (Fuster, 1989), mesial and dorsolateral prefrontal brain areas have been related to reflex inhibition in the antisaccade task (Gaymard et al., 1998; O'Driscoll et al., 1995; Pierrot-Deseilligny, Rivaud, Gaymard, Agid, 1991), the supplementary motor cortex was shown to be involved in both initiation and suppression of voluntary movements (Aron, Robbins, & Poldrack, 2004), DLPFC, IPFC and ACG are activated during the more cognitive/ attentional forms of "inhibiting interference" during the Stroop task (J. Z. V. Pardo, P.J. Pardo, Janer, Raichle, 1990; Bench et al., 1993; Taylor et al., 1997; Stuss, Floden, Alexander, Levine, Katz, 2001, Andres & Van der Linden, 2004). Inhibition of a motor response is the most direct expression of inhibitory control, as it involves (compared to the more cognitive forms of inhibitory control such as interference control) all-or-none decisions about action or non-action. Several brain areas have been related to inhibition of a motor response in stop and go/no-go tasks, including orbital, inferior, dorsolateral and mesial frontal, temporal and parietal cortices, as well as cerebellum and basal ganglia (Garavan, Ross, & Stein, 1999; Rubia et al., 1997, 1999, 2001; Andres & Van der Linden, 2004).

In this study we review recent evidence from behavioural studies of patients with unilateral PFC lesions. Lesion studies, unlike neuroimaging, can establish which brain regions are necessary for cognition, and advances in lesion-mapping technology, using structural MRI, allow better lesion resolution. Empirical evidence from studies with brain-damaged patients (Henson, Shallice, & Dolan, 1999; Rubia et al, 2003; Conway & Fthenaki, 2003; McDonald et al, 2006) supports the involvement of the frontal cortex (i.e. DLPFC, BA 9 and 46 and ACG, BA 24) in executive processes such as inhibition. The picture is not this straightforward however, and the univocal relation between these functions and the frontal cortex is still debated. With regard to the ability to inhibit irrelevant information, recent neuropsychological studies also failed to show impaired performance in patients with focal frontal damage in classical tests of inhibition such as the Wisconsin card sorting test (e.g. Fuster, 2001; O'Reilly, Noelle, Braver, Cohen, 2002) and the Stroop test (e.g. Goldman-Rakic, 1987). Thus, the question of which brain areas are involved in inhibitory control is still under scrutinity.

Given the importance of inhibitory control in managing overt behavior, the question arises whether internal actions might also be influenced by such mechanisms. Parallels exist between the control of action and the control of memory. Whithin the domain of memory, inhibitory mechanisms are thought to play an important role in the gating of irrelevant information from active work space during memory processing (e.g. Bjork, 1989; Zacks, Radvansky, & Hasher, 1996). Thus, inefficient inhibition could impede memory by taking up space and by consuming processing resources that could be used to help process and retrieve additional relevant information (Bjorklund & Harnishfeger, 1990). There are several neuropsychological accounts postulating that deficit in inhibition might underlie the memory impairments observed in patients with frontal lobe damage. Shimamura (1995), for example suggested that these memory impairments result from a failure to supress or inhibit irrelevant or erroneous search paths once they have been activated by internal or external stimuli. According to his theory, confabulations and intrusions that are often observed during recall in frontal lesion patients (Moscovitch & Melo, 1997), may occur because related memories are activated along with activation of the target memory. Thus, his theory focuses on inhibitory failures that occur primarily at retrieval. Other researchers have proposed that inhibitory failures in patients with frontal lobe damage account for their impairments on tests of recognition memory (via a high fales positive rate; Schacter, Verfaellie, Anes, Racine, 1998; Budson et al., 2002), semantic retrieval (Copland, Chenery, & Murdoch, 2000), and working-memory (Perlstein, Dixit, Carter, Noll, Cohen, 2003). Thus, it appears that a deficit in inhibition might help to account for the memory impairments often observed in patients with frontal lobe dysfunction. A substantial body of evidence indicates that when a selection is made between competing items in long-term memory, strongly competing unselected items are inhibited (see Bjork, 1998 for review). According to one opinion this inhibition occurs automatically when a choice is made between competitors (see for example, Anderson & Spellman, 1995; Conway, Harries, Noyes, Racsmány, Frankish, 2000; Anderson, 2003). However, the conditions that trigger inhibition may take different forms. For instance, an intention to forget (Bjork, 1989) or explicit and repeated attempts at forgetting (Anderson & Green, 2001) may under certain circumstances trigger inhibition, modulated by executive processes. In contrast, simply accessing an item from a set of items may automatically trigger inhibition without any intention to forget or suppress. In this latter case, when inhibition is triggered automatically, in the absence of an intention to forget, the executive processes may have less of a mediating role. One implication of this is that patients with brain injuries of those networks that support excutive processes in memory may have a reduced ability to generate the conditions that could trigger inhibition while still showing normal inhibition in tasks in which inhibition is triggered automatically. Although classical views of executive functions tend to locate these functions in the frontal cortex, more recent views suggest that executive functions might be sustained by a broader cortical neural network rather than by solely the frontal cortex (Andres & Van der Linden, 2002; Andres, 2003). In order to contribute to the distinction between these two views, we have limited our research to patients with focal lesions of the frontal lobes, and have attempted to characterize the lesion location and extent as exactly as possible in naturally occurring lesions in human patients. The purpose of the first four sudies in this section was to evaluate this hypothesis in patients with only unilateral frontal lobe injuries compared to a group with only unilateral temporal lobe injuries. We reasoned that frontal patients with impaired executive processes will have difficulties in intentional inhibition whereas this might not be the case for temporal patients with intact executive processes.

Bjork (1989) provides an example of how memory inhibition can benefit drivers when parking in a new spot every day. For today, it is useful to remember where the car is parked. But it is also useful to forget where the car was parked yesterday, as it prevents confusion about where the car is now. Intentional forgetting can help update memory for any changing information, like wrong directions, a switched meeting time, or a friend's new phone number. But is it equally effective for forgetting an ex-lover's phone number after a painful breakup? In the film *Eternal Sunshine of the Spotless Mind,* a corporation named Lacuna, Inc. has developed technology for the focused erasure of unwanted memories. Customers choosing this procedure all want to erase painful memories—ex-lovers, departed spouses, long-time pets. What happens when a person tries to forget an emotional past? Research suggests that the mind treats emotional events differently from mundane ones, often resulting in better recall when people try to remember. But emotional memories are also unique in another way. Sometimes, people do not want to remember. We have only the slimmest evidence about how intentional forgetting fairs against an emotional memory. Thus, the second studied issue in this section was the disturbance of inhibitory control, due to the effect of anxiety related emotions on executive processes.

There has been considerable interest in research into inhibitional biases for threat information in anxiety because recent cognitive theories have proposed that such biases may play a key role in the development and maintenance of clinical anxiety states (Rapaport, 1971; Mathews & MacLeod, 1994; Eysenck, 1992; Williams et al, 1997; Kulas et al., 2002). Cognitive models of anxiety propose that biases in processing threat-related information may cause or maintain clinical anxiety (e.g. Beck & Emery, 1985; Eysenck, 1997; Mogg & Bradley, 1998; Williams et al., 1988, 1997). Most of these studies have concerned clinical disorders and coping styles or the persons' trait anxiety level, mainly using a modified version of the Stroop paradigm, the emotional Stroop task (Mogg & Bradley, 1998; Williams et al., 1988, 1997). A few studies have examined intentional inhibition in the context of emotion. These studies have focused on *who* is likely to show enhanced or disrupted intentional inhibition of specific kinds of emotion-related memories. However, previous research has not addressed the fundamental relationship between emotion and intentional forgetting. Previous studies did show significant directed forgetting effects for pleasant, unpleasant, and trauma-related words, suggesting that emotional interference effect and intentional forgetting for emotional words is greater than zero. But the studies do not answer the question of whether emotional events resist intentional forgetting.

Thus, the purpose of the last two experiments from this section was to investigate the effects of anxiety related emotions on executive processes using two widely used inhibitional paradigms, namely the emotional Stroop task and the intentional forgetting task with emotion-related materials.

2. 1. Stroop performance in focal brain lesion patients

The Stroop test (Stroop, 1935) is one of the most widely used paradigms of experimental psychology and clinical neuropsychology, yet the neural basis of performance on the Stroop test is incompletely understood. The goal of this first study was to examine the effect of unilateral brain lesions, particularly frontal area, on the different processes involved in Stroop performance.

Multiple versions of the Stroop task exist. The classic version (Stroop, 1935) consists of three conditions: reading color words printed in black; naming the color of colored stimuli (e.g. XXXXX); naming the color of ink in which a color name is printed when the color is incongruent with the name ('red' printed in color blue, and the subject is asked to name the color instead of reading the word). The third condition elicits the standard 'Stroop-effect' – a significant slowing of performance. Thus the Stroop-task requires the deliberate stopping of a response (e.g. reading the word) that is relatively automatic. We used a computerized version of the Stroop task as described in the methods.

There are many methodologies of analysis of reaction time, however, error analysis of the Stroop task has not been common. Stroop (1935) used an arbitrary procedure of adding two times the average response time per item for each error; a technique copied by Gardner et al. (1959). Smith (1959) argued that no correction for errors was necessary because they are too infrequent in healthy adult subjects. Total time measure has not, however, been adequate to demonstrate the effect of brain injuries (Stuss et al, 2001). Brain disease may impair word or color processing or cause distractibility, bradykinesia, impulsivity, perseverations, or indifference, all qualities that should influence susceptibility to errors (Stuss, 1986; Stuss et al, 2001).

The neural basis for performance of the different conditions of the Stroop task is incompletely understood. Damage to left occipital or temporal stuctures would affect word or color recognition. Damage to the left temporoparietal structures would impair word production. Damage to the frontal lobes might result in a general slowing for all conditions. This could be secondary to damage in the left PFC, because of the linguistic – motor demands for all three conditions of the Stroop task (Stuss et al, 2001; Stuss & Levine, 2002). None of these observations is novel.

It is the disproportionately impaired performance on the incongruent condition that gives the Stroop task its power and interest. For the incongruent condition, damage to the prefrontal lobes should disrupt performance most. A major role of the frontal lobes is to control response options, through marshalling inhibitory processes, establishing response selection, or maintaining constant activation of the intended goal (Stuss, 1986; Stuss et al, 2001). It is not surprising that most research on localization of the brain structures required for the Stroop task has focused on the frontal lobes.

Many different studies have defined regions within the frontal lobes that may have more specific roles in processes necessary for the Stroop task. There are complementary studies from functional imaging in normal individuals and neuropsychological assessment of lesion effect.

From functional imaging different investigators have proposed a variety of frontal sites as key areas: left inferior lateral (Taylor, Kornblum, Lauber, Minoshima, Koeppe, 1997), left superiomedial (Pardo et al., 1990), right frontal polar (Bench et al, 1993), and bilateral anterior cingulate gyrus (ACG), perhaps with right predominance (Bench et al, 1993; Pardo et al, 1990). The repeated demonstration of medial frontal participation in the incongruent Stroop condition suggests a critical role for the ACG and/ or supplementary motor area (SMA). These experiments converge with abundant evidence that ACG is an essential structure for modulation of attention and intention, particularly for complex tasks (D'Esposito et al., 1995; Cabeza et al., 1997).

Lesion studies have also suggested different possible frontal regions: left lateral (Perret, 1974), right lateral (Vendrell et al., 1995; Kingma, Heij, Fasotti, Eling, 1996; Stuss et al., 2001; Stuss & Levine, 2002) and bilateral superiomedial (Holtz & Vilkki, 1988; Stuss et al., 2001).

There were three primary objectives in the present study: (1) to examine the usefulness of the Stroop interference effect as a measure of inhibitory control dependent on the PFC; (2) to investigate the possibility of distinct lesion effects for word reading or color naming; (3) and to specifically determine the laterality of the brain regions necessary for the performance of the incongruent condition.

2. 1. 1. Method

2. 1. 1. 1. Design

A 3 x 4 mixed factorial design was used with Stroop conditions (color-naming/ reading/ interference) as a within-subjects factor and Group (Right Frontal/ Left Frontal/ Temporal/ Control) as a between-subjects factor. The dependent variables were the RT and errors.

2. 1. 1. 2. Participants

The sample of 48 participants was composed of thirteen patients with right frontal lobe lesions, ten patients with left frontal lobe injuries, twelve with unilateral temporal lesions (six left and six right) and thirteen control subjects. The patients were recruited from the National Institute for Medical Rehabilitation, Head- and Brain Injury Department, in Budapest, Hungary, identified by review of their medical records, consisting in computer tomography (CT) or magnetic resonance (MRI). Patients met the following inclusion criteria: presence of a single focal unilateral frontal or temporal lesion, time since onset greater than 1.5 months. Specific details of lesions sites were not available and the medical notes indicated only laterality of injury and general extension. It should be noted, that patients were selected because their records indicated only frontal or temporal injuries, but it is, however, possible that minor lesions went undetected, and this is especially possible in the patients with closed head injuries. This could be a potential problem although it should be emphasized that their medical records indicated only frontal or temporal lobe pathology. Table 2. 1. presents the patient's characteristics. The right frontal patients averaged 27.38 years of age (range 17 - 46) and 12.62 years of education (range 8 - 17 years); the left frontal group had an average 33.30 years (range 16 - 60) and 12.10 years of education (range 8 - 17). The mean age and educational level for the temporal group were 32 years (range 16 - 48) and 11.67 (range 8 - 16) respectively. The 13 healthy volunteers (7 male and 6 female) were matched approximately with the patients on the basis of age, education and IQ. Their average age was 23.62 years (range 17 - 32) and time spent in education was 12.69 (range 8 - 17 years). Comparing the demographic data of the groups, nor the age differences, $F(3, 44) = 2.42$, $p > .05$), nor educational differences, $F(3, 44) = .59$, $p > .05$, were significant.

Table 2.1. Demographical and neuropsychological characteristics of the groups

	Subjects with right-sided frontal cortex lesion (N = 13)	Subjects with left-sided frontal cortex lesion (N = 11)	Subjects with unilateral temporal cortex lesion (N = 12)	Control subjects (N = 13)
Age (years)	27.38 (7.75)	33.3 (15.43)	32.00 (9.92)	23.62 (4.89)
Education (years)	12.62 (2.26)	12.12 (3.07)	11.67 (1.50)	12.69 (1.80)
Sex, male: female	7 : 6	9 : 2	6 : 6	7 : 6
Lesion aetiology, TBI: EP : AVM: cyste	12 : 0 : 1 : 0	9 : 0 : 0: 1	11 : 1 : 0 : 0	
Lesion location, right : left	13 : 0	0 :13	6 : 6	

Note: Table values are mean (S.D.). Traumatic Brain Injury; EP: Epilepsy; AVM: Anterio-venous malformation.

2. 1. 1. 3. Materials

A computerized version of the Stroop task was used, with three conditions: color-naming, reading and incongruent color naming. The color naming condition consisted in 60 XXXXX items colored red, blue, green or yellow. The reading condition consisted from 60 color-name words (RED, BLUE, GREEN, YELLOW) written with black ink, and the interference condition was the standard Stroop incongruent color naming condition: the words RED, BLUE, GREEN, YELLOW were written 60 times in a color that differed from the word meaning.

2. 1. 1. 4. Procedure

Participants were tested individually, lasting approximately 10 - 15 minutes. For the Stroop task the subjects were instructed to read the words (reading condition) or name the color of the stimuli as quickly and as accurately as possible (color naming and incongruent color naming conditions), and to give a correct motor response (pressing the adequate button). Before the test phase the subjects performed a pretest with twelve stimuli to check that they have comprehended the task, to make themselves familiar with the task conditions and to practice the adequate motor responses (e.g. to learn the buttons' position corresponding to all four colors). In the test phase the three experimental conditions were divided in six blocks. The order of items within blocks and the order of blocks presentation were random for each subject. The time spent on each of the items was recorded and the mean RT for each condition was calculated, recording also the errors as an indicator of accuracy.

2. 1. 2. Results and Discussion

A 4 x 3 two-way ANOVA was carried out with one between-subjects variable (groups) and one within–subjects variable (Stroop conditions) for RT as dependent variable. The interaction effect of two variables was not significant, $F (6, 82) = .49$; $p > .05$, but a significant main effect was found for group variable, $F (3, 42) = 4.18$; $p < .05$ and for Stroop conditions, $F (2, 82) = 39.58$; $p < .01$.

This analysis also revealed a significant interaction effect, taking the errors as dependent variables, $F (6, 82) = 2.68$; $p <0.05$, and the main effects for group variable, $F (3, 42) = 3.8$; $p = .01$, and for Stroop conditions, $F (2, 82) = 7.82$, $p < .01$, were significant too.

For further analysis we have compared the groups with one-way ANOVA with reaction times as dependent variable (see Table 2.2.) and we found significant differences in color name conditions, $F(3, 44) = 3.93$, $p < .05$, but no significant differences were found in reading condition, $F(3, 44) = 2.57$, $p > .05$ and in interference condition, $F(3, 44) = 1.9$, $p > .05$. A post-hoc Scheffe analysis revealed that this difference in color naming and in reading conditions was found between the healthy controls and temporal lobe injured group, possibly due to the general slowering of information processing and motor responses in patients.

Analyzing the errors with one- way ANOVA, we found a significant difference only in the interference condition, $F(3, 44) = 4.56$, $p < .05$, while in the other two conditions the differences were not significant, $Fs < 1.5$. Post-hoc Scheffe analysis showed that the right frontal group produced significantly more errors than other patients and control groups (see Table 2. 2).

Table 2. 2. RT and errors in Stroop - conditions

	Right Frontal lesion group (N = 13)	Left Frontal lesion group (N = 11)	Unilateral temporal lesion group (N = 12)	Control group (N = 13)
Color Naming (RT in msec)	1684 (506)	1383 (229)	1791 (716)	1212 (224)
Reading (RT in msec)	1537 (279)	1419 (173)	2160 (1864)	1196 (225)
Interference (RT in msec)	2128 (630)	1869 (359)	2092 (1070)	1545 (362)
Color Naming (errors)	2.31 (3.68)	.60 (1.26)	1.56 (1.94)	.77 (.83)
Reading (errors)	.92 (2.78)	.10 (.31)	.11 (.33)	.46 (.51)
Interference (errors)	6.31 (7.50)	1.10 (.99)	1.56 (2.18)	1.23 (1.23)

Note: Table values are mean (S.D.).

Two interference indices (one for the RT and the other one for the errors) were calculated by subtracting for each participant the reaction time or errors in the color naming condition from the reaction time or errors in the interference condition. These interference indices were submitted to one-way ANOVA analysis. For reaction time no differences were found between the groups, $F(3, 44) = .46$; $p > .05$ (see Figure 2. 1 a). On the other hand the comparison of the interference index for errors revealed a tendency toward a significant difference, due to the differences between right frontal and the other groups, $F(3, 43) = 2.49$, $p < .1$ (see Figure 2. 1b).

We have analyzed with two-way ANOVA the separate effect of laterality and the localization, and only the interaction effect of two variables was significant, $F (1, 34) = 3.79$, $p < .05$ for the RT.

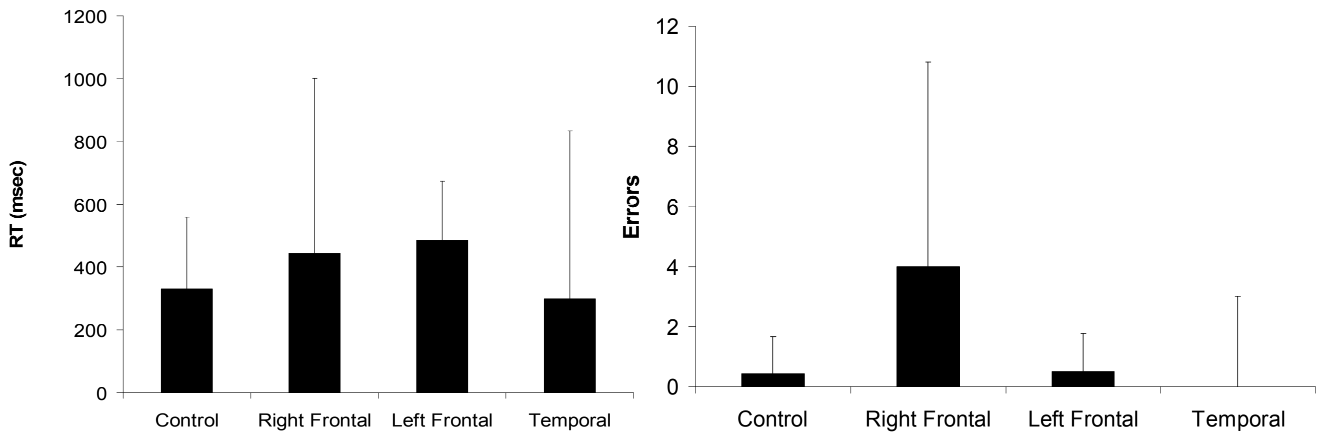


Figure 2. 1. Interference Indices in the Stroop task. **2. 1a**. Interference Index for RT. **2.1b**. Interference Index for errors.

In summary, the data indicates that subjects with right frontal lesion showed a remarkable interference effect, making significantly more errors in interference condition even though they were explicitly instructed to ignore the semantic content of the words. This finding is in line with previous studies demonstrating a higher interference effect in frontal lobe injured persons (Vendrell et al, 1995; Stuss et al., 2001, Stuss et al, 2002), but in our study this sensitivity to interference could be observed especially in frontal patients with right lateralization. Similarly, the interference index calculated from errors seems to be more sensitive to the right frontal injuries. This interference effect in right frontal patients could be seen only in error rates, because the reaction times of all patient groups were quite similar, differing only from the control groups' reaction time. This may be due to a generally slowered information processing and affected motor responses after brain injuries. The impaired patients in each condition were also generally slower, but some frontal patients who did not make errors were also slow. Thus, it can be conluded that time scores alone may not be the most effective measure of Stroop performance.

2. 2. Go/ no-go performance in focal brain lesions patients

In our second study a go/ no-go task was used with the aim to investigate the inhibitory control with a simple response inhibition paradigm. Response inhibition is the cognitive process required to cancel an intended movement. The subject is required to perform a speeded response in go trials and to inhibit responding on no-go trials. The task demands high-level cognitive functions of response-selection and response inhibition. For go/no-go tasks the index of inhibitory control is the number of errors a subject makes on no-go trials (i.e. going when they should not) (Rubia et al., 2001).

In neuroimaging studies response inhibition consistently and especially activates a right-lateralized inferior frontal cortex (IFC) region (deJong, Coles, & Logan, 1995; D'Esposito et al, 1995; Konishi, Nakajima, Uchida, Sekihara, Miyashita, 1998; Konishi. et al., 1999; Garavan Ross, & Stein,1999; Menon, Adleman, White, Glover, Reiss, 2001; Bunge, Dudukovic, Thomason, Vaidya, Gabrieli, 2002; Garavan, Ross, Murphy, Roche, Stein, 2002; Rubia, Smith, Brammer, Taylor, 2003; Aron, Robbins, & Poldrack , 2004) and this region (but no other regions of the right or left PFC) was shown to be crucial by a neuropsychological study of patients with unilateral right-PFC damage (Aron, Robbins, & Poldrack , 2004).

Overall, in neuroimaging studies it seems that response inhibition consistently and especially activates a right-lateralized inferior frontal cortex (IFC) region (Garavan Ross, & Stein, 1999; Garavan et al, 2002; Aron, Robbins, & Poldrack , 2004).

Thus, the goal of this lateralization study was to further investigate and compare the neurocognitive networks related to go/no-go task, by comparing performance of unilateral frontal lobe injured- and temporal lobe injured patients.

2. 2. 1. Method

2. 2. 1. 1. Design

Two 2 x 4 mixed factorial design was used with go/ no-go conditions (go and no-go) as a within-subjects factor and Group (Right Frontal/ Left Frontal/ Temporal/ Control) as a between-subjects factor. The dependent variables were the RT and false alarms.

2. 2. 1. 2. Materials

The go/ no-go task requires selection of either a motor response by pressing a button, indicated by a go signal, or a "no-response," indicated by a no-go signal. A computerized go/ no-go task was used, with five different visual stimulus patterns presented 60 times in random order, and only two of them required go responses (24 times). In this manner go signals and no-go signals alternated with 40% and 60% probability each. All stimulus patterns consisted in a black square with white dots and lines, differing only in the pattern formed by their arrangement. Interstimulus-interval (ISI) was 1000 ms, including a stimulus duration of 200 ms followed by a blank screen for 800 ms.

2. 2. 1. 3. Procedure

Participants were tested individually, lasting approximately 10 - 20 minutes.

In go/ no- go task the subject is required to perform speeded responses on go trials (e.g. pressing the button in response to the target stimulus/ stimuli) and to inhibit responding on no-go trials (non target stimuli). Before starting the experimental tasks, they performed a pretest to make them familiar with the task conditions and to practice the motor response (pressing the button). The subjects first had to memorize the target stimuli, and then they performed the pretest, and finally the original experimental task. At the end, the participants were debriefed.

2. 2. 2. Results and Discussion

Two one-way ANOVAs were carried out with groups as independent, and reaction times (RT) and false alarms as dependent variables, both taken as indices of inhibitory control (disinhibition indices) (see Table 2. 3). We found significant differences in RT, $F(3, 42) = 6.04$; $p < .01$, and post-hoc Scheffe analysis revealed that the right frontal group was significantly slower than the other groups.

However, analyzing the false alarms we found only a strong tendency toward the significance, $F(3, 44) = 2.61$; $p = .06$, with the right frontal group producing the highest rate of false alarms (see Fig. 2. 2). Taken together these two results we can assume that the right frontal group, due to the impaired inhibitory motor control, first produced false alarms and after a while by learning the goal stimuli showed "only" a higher RT go conditions.

We have separated the effect of laterality and the localization on the two interference indices and the interaction effect was significant for both RT, $F(1, 34) = 5.19$, $p < .05$ and false alarms too, $F(1, 34) = 3.2$, $p < .01$. The main effect of localizations was also significant for the false alarms only, $F(1, 34) = 1.25$, $p < .05$.

Table 2. 3. The number of correct responses and RT in the go/ no-go task

	Right Frontal lesion group (N = 13)	Left Frontal lesion group (N = 11)	Unilateral temporal lesion group (N = 12)	Control group (N = 13)
Number of Hits (max. 24)	19.66 (5.58)	19.50 (4.92)	21.75 (3.13)	23.50 (.52)
RT for Hits (msec)	824 (273)	711 (106)	6.99 (153)	530 (66)

Note: Table values are mean (S.D.).

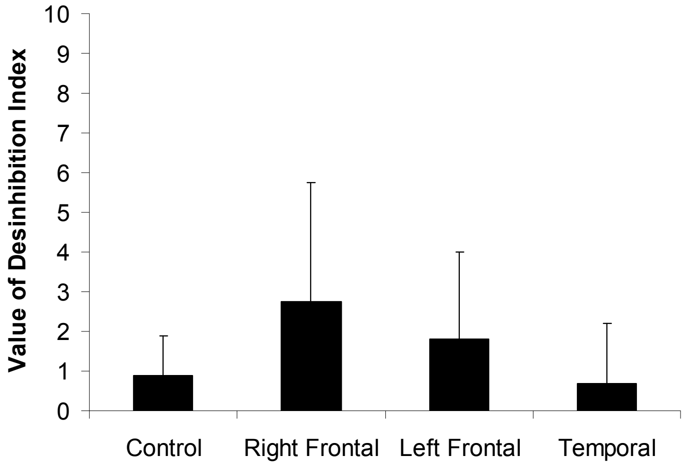


Fig. 2. 2. Desinhibition index (False Alarms) in the go/ no-go task.

To summarize, the results demonstrate that patients with right frontal lesion showed no inhibitory effect in go/ no-go task, while other patient groups produced task-required inhibition. The right frontal group, due to the impaired inhibitory motor control, first produced false alarms and after a while by learning the goal stimuli showed "only" a higher RT. This result is in concordance with the results of previous neuroimaging studies (D'Esposito et al, 1995; Konishi et al., 1998; Konishi. et al., 1999; Garavan et al., 1999; Menon et al., 2001; Bunge et al., 2002; Garavan et al., 2002; Rubia et al., 2003; Aaron et al, 2003; Aaron et al., 2004).

2. 3. Directed forgetting effect in focal brain lesions patients

Within the domain of memory, inhibitory mechanisms are thought to play an important role in blocking of irrelevant information from active work space during memory processing (e. g. Bjork, 1989).

In many types of everyday situations individuals are cued to set aside, get rid of, supress, either permanently, either definitively something that resides in memory (E. L. Bjork, Bjork, & Anderson, 1998). Although forgetting is most often viewed as having negative effects, to function efficiently in our everyday environment, we frequently need to forget or inhibit previous information.

With regard to lesion studies, only a few of them have investigated the influence of inhibitory mechanisms on the memory performance of patients with brain injury (Andres & Van der Linden, 2002; Conway & Fthenaki, 2003; Schmitter-Edgecombe, Marks, Wright, & Ventura, 2004; McDonald et al., 2006). This is an important area of research because the ability to supress irrelevant information can be as important in attaining goals as to remember task-relevant information. The results from previous lesion studies are controversial: some of them provided evidence for normal directed forgetting (DF) effect in brain injuried populations, regardless of their lesion site (e.g. Andres & Van der Linden, 2002; Andres, 2003; Schmitter-Edgecome et al., 2004), other studies found evidence either for left frontal involvement (McDonald et al., 2006), or for the role of the right frontal lobe in the inhibitory memory control (Conway & Fthenaki, 2003). However, the only lesion study using the RIF paradigm found normal RIF effect in all frontal patients regardless of their lesion site (Conway & Fthenaki, 2003).

In the present study, we used a DF task to examine the role of inhibition in memory performance following lesion to the unilateral frontal and temporal lobes.

Directed forgetting tasks have emerged as the primary way to investigate „intentional forgetting" in the laboratory (Bjork, 1968; Woodward & Bjork, 1973; Bjork, 1989; MacLeod, 1999). Research on intentional forgetting shows that people can forget certain information when they want or are instructed to do so. There are two basic DF paradigms: the item method and the list method (Basden, Basden, & Gargano, 1993). In the item method, each item in a list is presented for a period of study and designated either „to be forgotten" (TBF) or „to be remembered" (TBR). In the list method participants study a list of words with instructions to remember them for a later recall test. In one condition (Forget condition) after learning the words participants are told to forget them and concentrate on learning a second list. In the other condition (the Remember condition) participants are told to remember both lists of words. On a later recall test participants are asked to recall words on both lists, ignoring any previous instructions to forget. There are two consistent effects in this kind of task. First, participants in the Forget condition recall fewer words from the to-be-forgotten list, than in Remember condition, which is evidence for intentional forgetting. The second result is observed in better recall of words from the second list in Forget condition, than from the Remember condition. This finding provides evidence that participants in Forget condition do not have the first list as a source of interference. These two results are called directed forgetting (DF) effect, which can be explained by two possible mechanisms. Some theories emphasize selective remembering rather then selective forgetting, especially in case of the item method. Bjork (1968, 1989) for example, has discussed the possibility that two interrelated processes might be operating during encoding which could largely account for the pattern of findings. The alternative explanation of DF effect, especially explaining the list method effect, emphasizes the role of active, intentional and goal-oriented inhibition at retrieval level (Bjork, 1989; Basden, Basden & Gargano, 1993; Johnson, 1994; Racsmány & Conway, 2006).

Given our interest in investigating memory inhibitory mechanisms in a population with brain injury, we used a variant of the list method DF procedure in this study. Thus, participants took part in a directed forgetting (DF) experiment using a standard list method. This was a within-subjects procedure with four lists: F list 1, F list 2, R list 1 and R list 2. Each is studied in pairs and then freely recalled. The standard DF effect is seen in poor recall of F list 1 relative to F list 2 and R list 1 and is usually only found in free recall (MacLeod, 1998). Directed forgetting with list is a more direct test of memory inhibitory processes, because the forgetting effect is caused by inhibition of F list 1, rather then reduced rehearsal (Bjork, 1989; Bjork et al., 1998; Conway et al. 2000; Conway & Fthenaki, 2003).

2. 3. 1. Method

2. 3. 1. 1. Design

A 2 x 4 mixed factorial design was used with Instruction type (Remember/ Forget) as a within-subjects factor and Group (Right Frontal/ Left Frontal/ Temporal/ Control) as a between-subjects factor. The dependent variable was the recall rate.

2. 3. 1. 2. Materials

Thirty-two unrelated common nouns were selected according to the following criteria: all words had 4-6 letters, they were semantically unrelated and had an approximately equal word frequency (corpus *szoszablya.hu* was used for word frequency equation). The words were randomly allocated to four lists of eight words for the study phase. Two lists were randomly assigned to the Forget-Remember condition while the other two were allocated to Remember-Remember condition and the order of the lists and conditions was rotated across participants. The words were presented on a computer screen, each word appearing for 3 seconds. Between the study and recall phase a 3- minute paper and pencil arithmetic task was administered.

2. 3. 1. 3. Procedure

Participants were tested individually, lasting approximately 15 - 20 minutes. This DF procedure consisted of three phases: (a) study, (b) a filled interval, (c) free recall. In the study phase after the presentation of list 1 a remember (R) cue or forgetting (F) cue was given, and then the list 2 with remember instruction. After three minutes filled interval in the free oral recall test, the subjects were requested to try to remember the words previously seen in the study phase, regardless which cue, R or F has originally been given. The recall test was terminated when the participant could not remember any more words, or when a 3 - minute interval had passed. Participants were debriefed at the end of the study.

2. 3. 2. Results and Discussion

A mixed three-factor ANOVA was performed with groups (right frontal, left frontal, temporal and control) as a between-subject factor, and instruction type (remember/ forget) and list (list 1 / list 2) as within subject factors. The tree-way interaction was significant, $F(1, 45) = 2.77$, $p = .05$, and also the instruction x list interaction effect, $F(1, 45) = 6.78$, $p = .01$. None of the other two-way interactions reached significance, $Fs < 1.8$. The analysis revealed a significant main effect of the groups, $F(1, 45) = 10.87$, $p < .001$, but the other two main effects were not significant statistically, $Fs < 1.6$.

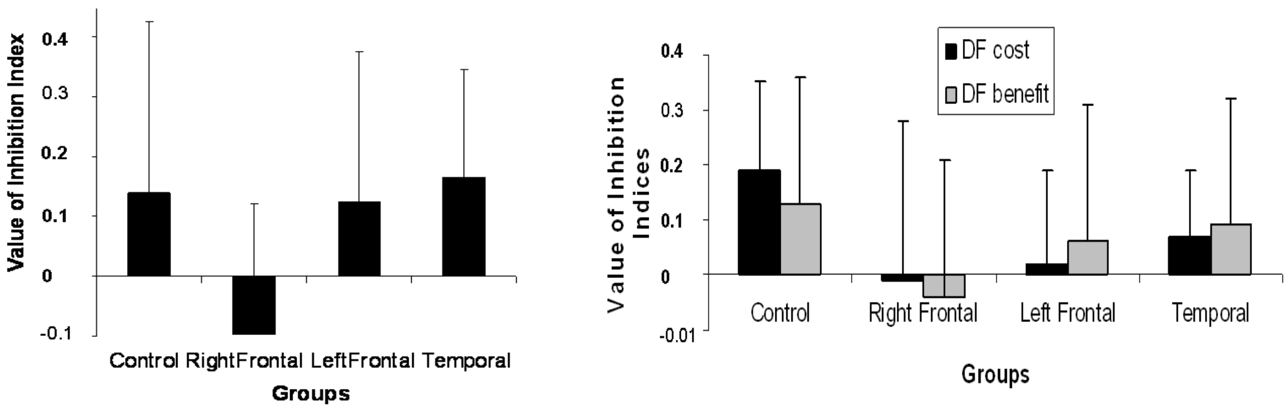
The standard DF effect can be seen in poor recall rate of F list 1 relative to F list 2 and R list1. For the control group (as it can be seen in Table 2. 4) a standard DF effect was observed: the critical contrast between F list1 and F list 2 was significant, $t(11) = 3.11$, $p = .01$, and the comparison of F list 1 with R list 1 was significant, $t(11) = 3.97$, $p < .01$, too. For the temporal lobe group a poorer recall rate with an attenuated, but otherwise a normal DF effect was found: F list1 versus F list 2, $t(11) = 3.2$, $p < .01$, and F list1 with R list 1, $t(11) = 1.97$, $p > .05$. For the left frontal group neither the first comparison $t(9) = 1.58$, $p > .05$, nor the second, $t(9) = .45$, $p > .05$ was significant, despite the means being in the expected direction. Finally, for the right frontal group a reverse pattern can be observed: they have recalled more words from F list1 than F list 2, although the critical comparisons were not significant: t (12) =1.59, p > .05, and the second, t (12) = 0.11, p > .05, respectively. These results suggest a rebound effect in the right frontal group, in which items targeted for inhibition are recalled to unexpectedly high levels.

Table 2. 4. Recall rate of groups in DF paradigm

	Right Frontal lesion group (N = 13)	Left Frontal lesion group (N = 11)	Unilateral temporal lesion group (N = 12)	Control group (N = 13)
F List 1	.23 (.17)	.17 (.10)	.11 (.11)	.30 (.19)
F List 2	.13 (.90)	.30 (.21)	.28 (.20)	.53(.22)
R List 1	.22 (.20)	.20 (.17)	.18 (.18)	.50 (.16)
R List 2	.18 (.18)	.23 (.25)	.24 (.23)	.39 (.28)

Note: Table values are mean (S.D). F : Forgetting condition; R : Remembering condition

An inhibition index was calculated according to Conway and Fthenaki (2003) calculation method by subtracting Forgetting List 1 from Forgetting List 2 items for each participant. This DF index was compared with one-way ANOVA, using the group variable (see Fig. 2. 3a). Mean values vary between -1 and 1 with score of zero or bellow zero indicating no inhibition and score 1 of one indicating total inhibition. One-way ANOVA revealed a significant difference between groups, F (3, 44) = 4.40, p < .01, and post-hoc Sheffe-test showed that this difference was due to the right frontal group's inability to inhibit Forgetting List 1 items, while all the other groups showed some degree of inhibition. We have calculated two further inhibition indices, frequently used in literature: a DF cost index, by subtracting for each participant Forgetting List1 from Remember List1 items and DF benefit index, by subtracting Remember List 2 from Forgetting List 2. These indices were compared with one-way ANOVAs, using the Group variable (see Fig. 2. 3b). Comparing the performance of all four groups, the differences between groups for the DF benefit index was not significant, F (3, 44) = 1.35, p > .05 and for the DF cost index the difference shows a tendency toward significance F (3, 44) = 2.43, p < .1. We tested this tendency with further analysis comparing the groups with paired t-test. For control- right frontal groups comparisions we found a significant difference for the DF cost index, t (24) = 2.17, p < .05, but for the DF benefit index the difference showed only a tendency toward significance t (24) = 1,92, p< .1. Comparing the control and left frontal groups the difference for the DF cost index was significant, t (21) = 2.34, p < .05, but for the DF benefit index not, t (21) = .71, p > .05. Finally, for control- temporal groups comparision none of the differences reached significance: t (23) = 2.01, p< .1; t (23) = .44, p > .1, but as it can be seen, for the DF cost index the difference showed a tendency toward significance.



] **Figure 2. 3.** Inhibition Indices in DF paradigm. **Fig. 2. 3a**. DF inhibition index (F list 2 – F list 1) calculated after Conway and Fthenaki (2003). **Fig. 2. 3b.** DF cost (R list 1 – F list 1) and DF benefit (F list 2 – R list 2) indices. Mean values of inhibition indices vary between -1 and 1 with a score of zero or bellow of zero indicating no inhibition and score of 1 total inhibition.

For further analysis we have analyzed the separate effects of laterality (right or left) and localization (e.g. frontal or temporal) with two-way ANOVA. The interaction effect of two variables was significant, F (1, 35) = 3.07, p < .05, and a significant main effect was found for the lateralization variable, F (1, 35) = 3.91, p = .05. The effect of localization was not significant F (1, 35) = 6.38, p >.05.

In summary, the findings show that the DF manipulation did not lead to enhanced recall of TBR items with impaired recall of TBF items for the right frontal group, while the left frontal group showed an attenuated DF effect. In contrast to the right frontal group a robust directed forgetting effect was found in temporal and the control groups. Especially the right frontal lobe group may have a particular difficulty in intentionally inhibiting the memory items, designated for forgetting, and they may even suffer from some sort of “rebound” effect in which intentionally unattended items intrude into awareness (Wegner, 1994). The laterality differences between the left- and right frontal groups suggest that problems in intentional inhibition are more strongly associated with lesions of the right compared to the left cortical hemisphere.

2. 4. Retrieval induced forgetting effect in focal brain lesions patients

The aim of this study was to examine the automatic inhibition that occurs in the retrieval induced forgetting procedure (RIF, Anderson & Spellman, 1995).

Anderson, Bjork and Bjork (1994) produced compelling evidence that the cued recall of an item can impair later recall of items previously associated to the same cue, and this phenomenon was labelled retrieval-induced forgetting (RIF) effect. According to Anderson and his colleagues (Anderson & Spellman, 1995) an important property of RIF effect is cue-independence, i.e. the inhibition caused by retrieval generalises to any other cue used to test that item. This means that the forgotten competitive item itself is impaired by an active suppression when a related target is sufficiently retrieved (Anderson & Neely, 1996). An another critical property of the RIF effect is the recall-specifity, i. e. retrieval practice impairs the delayed recall of competing items, but the same number of repeated study exposures does not. Consistent with this, when retrieval practice is performed, the amount of impairment often has no relation to the amount of streghtening observed on practiced items, thus RIF appears to be strength-independent. However, impairment does appear to be interference-dependent (Anderson & Spellman, 1995).

Anderson and his colleagues developed a three-phase paradigm to study the mechanism of how memory retrieval impairs interfering memories (Anderson, Bjork & Bjork, 1994; Anderson, & Spellman, 1995; Anderson & McCulloch, 1999). In the study phase of this procedure subjects study lists of category-exemplar pairs (e.g. fruit – orange, fruit – banana, animal- tiger), and then perform retrieval practice on half of the exemplars from half of the categories by completing cued-stem recall tests (e.g., fruit-or___). This manipulation causes inhibition of unpracticed exemplars from practiced categories, detected in poor recall rates for these exemplars relative to recall of exemplars from unpracticed categories, and to practiced exemplars themselves. In the example above recall of ’Banana’ would be abolished relative to recall of ’Tiger’, and recall of ’Orange’ would be enhanced relative to exemplars from an unpracticed category.

According to Anderson and his colleagues, the impaired recall performance of competing unpractised items reflects the operation of an active suppression mechanism (Anderson & Spellman, 1995; Anderson & Neely 1996). This account is in agreement with many inhibitory theories in interference literature, which assume that active deactivation of interfering items plays an important role in human forgetting (e.g. Carr & Dagenbach, 1990; Dagenbach & Carr, 1994; Zacks & Hasher, 1994).

Recent neuroimaging findings (Anderson et al., 2004) further establish that controlling awareness of unwanted memories is associated with increased dorsolateral PFC activation, reduced hippocampal activation, and impaired retention of the unwanted trace, and that the magnitude of activation in PFC predicts memory supression. These findings indicate that cognitive and neural systems that support our ability to override prepotent responses can be recruited to override declarative memory retrieval, and that this cognitive act leads to memory failure. However, the only lesion study using the RIF paradigm found normal RIF effect in all frontal patients regardless of their lesion site (Conway & Fthenaki, 2003).

Thus, the aim of this lesion study was to find out whether or not frontal patients will show impaired inhibition in this less intentionally initiated form of inhibition.

2. 4. 1. Method

2. 4. 1. 1. Design

A similar design was employed as in Anderson & Spellman (1995) Experiment 1. Two factors, Retrieval practice condition, as a within- subjects factor and Group (patients), as between-subjects factor were used. Retrieval practice condition had three levels: (1) Rp+ items, were the exemplars practiced three times in category -cue-plus-stem-recall practice test (e.g., Fruit-Or____), (2) Rp- items, which constituted the unpracticed exemplars from the same, practiced categories as the Rp+, and (3) Nrp items, which were exemplars from unpracticed categories. The dependent variable was the number of exemplars correctly recalled in a cued recall test.

2. 4. 1. 2. Materials

Eight categories, two of which were fillers, with six exemplars from each category were selected. Each exemplar consisted of a two-syllable noun with approximately equal word frequencies (corpus *szoszablya.hu* was used for word frequency equation). In the learning phase the category – exemplar pairs were presented on a computer screen, each pair appearing 5 seconds in a random order with the restriction that no two categories appeared sequentially more than once. After the learning phase, a paper and pencil retrieval practice test was given to subjects in the following manner: the category name was presented in bold upper-case letters with the first two letters of the exemplars followed by a solid line, e.g. Fruit – Or____. The order of the retrieval practice items was random and was preceded and followed by filler items. The cued recall test contained the category cues with each cue being presented separately at the top of a page. The order of the categories was random.

2. 4. 1. 3. Procedure

Participants were tested individually, lasting approximately 40-60 minutes. This RIF procedure hadfour phases: (a) study, (b) retrieval practice, (c) filled interval, and (d) cued recall. In the first phase participants studied a list of category exemplars drawn from different categories, like Banana, Cherry, etc. The study phase was followed by a retrieval practice phase in which participants were allocated randomly to one of the six practice orders. The task was to recall the specific exemplars to category cues. In this phase three items from three experimental categories were practiced three times, and the exemplars from filler categories were recalled to category cues, too. Between the study and recall phase a 5 - minutes paper and pencil arithmetic task was administered. After the filled interval in the cued recall phase the subjects had to recall all the exemplars to category cues. The recalled words were differentiated to RP+, which are the practiced exemplars from the practiced categories, or RP-, which are the non-practiced items from the same practiced categories, and finally, Nrp items are the non-practiced exemplars from the non-practiced categories.

2. 4. 2. Results and Discussion

A mixed two-way ANOVA was performed with groups (right frontal, left frontal, temporal and control) as a between-subject factor, and retrieval practice (Rp+, Rp-, Nrp) as within-subject factor. The interaction effect was significant, $F (1, 45) = 3.27$, $p < .05$. The analysis revealed a significant main effect of the groups, $F (1, 45) = 4.05$, $p < .05$, but the main effect of retrieval practice showed only a tendency, $F (1, 45) = 2.83$, $p < .1$

The standard RIF effect can be detected in poor recall rates for RP- exemplars relative to recall of exemplars from unpracticed categories (Nrp), and of course to the practiced exemplars themselves (Rp+). Cued-recall rate of the four groups in the different retrieval practice conditions is shown in Table 4. The control group showed the expected pattern: the contrasts Rp+ versus Rp-: t (11) = 7.32, p < .001; Rp+ versus Nrp: t (11) = 4.98, p < .001 and for Rp- versus Nrp: t (11) = 5.41, p < .001, were all significant.

For the right frontal group Rp+ performance was reliably higher than Rp-, t (12) = 12.12, p < .001, and Nrp, t (12) = 10.40, p < .001, and also Rp- was reliably lower than Nrp, t (12) = 6.91, p < .001. Thus, right frontal patients showed a normal pattern of increased recall of practiced exemplars with inhibition of unpracticed items. A similar pattern was found in the left frontal group too: all of the contrasts were significant: Rp+ versus Rp- t (9) = 7.58, p< .001, Rp+ versus Nrp t (10) = 7.99, p< .001 and for Rp- versus Nrp t (10) = 4.19, p < .01. Temporal patients recalled Rp+ items to a significantly higher level than Rp- items, t (11) = 6.88, p < .001, and Nrp items, too, t (11) = 7.95, p < .001 and the difference between Rp- and Nrp items was significant, t (11) = 2.95, p < .01 (see Table 2. 5).

Table 2. 5. Recall rate of groups in RIF paradigm

	Right Frontal lesion group (N = 13)	Left Frontal lesion group (N = 11)	Unilateral Temporal lesion group (N = 12)	Control group (N = 13)
Rp+	.69 (.18)	.61 (.20)	.64 (.18)	.76 (.28)
Rp-	.11 (.08)	.08 (.09)	.17 (.16)	.20 (.16)
Nrp	.30 (.10)	.23 (.11)	.29 (.11)	.42 (.10)

Note: Table values are mean (S.D.). RP+: retrieval practice plus items; RP- : retrieval practice minus items; Nrp : non-retrieval practice items

An inhibition index was calculated by subtracting Rp- cued recall rate from Nrp rate for each participant, and this index was compared with one-way ANOVA, using the group variable (see Figure 2. 4). Mean values vary between 0 and 1 with a score of zero indicating no inhibition and a score of 1 total inhibition. Comparing the performance of all four groups, no difference was found between the groups, F (3, 44) = 1.19, p >.05.

We have analyzed with a two-way ANOVA the separate effect of laterality and the localization. The interaction effect of the two variables was not significant, F (1, 35) = .51; p > .05, and the main effects for lateralization and localization variables were not significant either, F (1, 35) = .37, p > .05 and F (1, 35) = .80, p > .05, respectively.

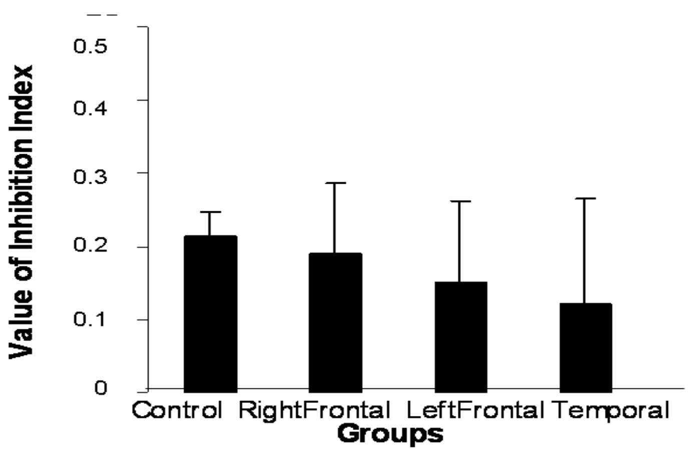


Figure 2. 4. Inhibition Index (NRp – Rp-) in RIF paradigm. Mean values vary between 0 and 1 with a score of zero indicating no inhibition and a score of 1 total inhibition.

Overall, the patterns of findings show an intact RIF for both the frontal- and temporal groups. The main conclusion to be drawn from the data is that frontal lobe patients do not show disrupted inhibition in RIF in contrast to their performance on intentionally initiated DF tasks, where severe impairment was observed, especially in patients with right side lesions.

2. 5. Emotional Stroop effect

To understand cognitive biases of attention in clinical disorders, psychological theories and clinical research have adapted an information processing paradigm derived from experimental cognitive psychology. The modified version of the Stroop task is the paradigm most frequently used to show attentional biases in anxiety patients. In this task participants are asked to name the ink color of words by ignoring their content. The basic finding is that, compared to other words and other participants, individuals with high anxiety are slow in color naming of anxiety-relevant words (Matthews & MacLeod, 1994; Richards & Whittaker, 1990; Mogg & Marden, 1990; Mogg et al, 1990; Richards, 1991; Richards et al, 1992; Matthews & MacLeod, 1994; French et al, 1996; Williams et al., 1997; Leung et al, 2000; Mogg et al, 2000; Albu, 2005; Albu, 2007). Presumably, anxiety relevant words have emotional meaning, creating an „attentional bias" that interferes with the color-naming task, although the precise nature of this mechanism remains unclear.

The modified emotional Stroop task has been used successfully with a variety of anxiety patients, among them patients with panic disorder (Ehlers et al, 1988; McNally et al, 1990; McNally et al, 1992), posttraumatic stress disorder (Foa et al, 1991; Kaspi et al., 1995), obsessive–compulsive disorder (Shoyer & Foa, 1991), specific phobia (Lavy, van den Hout, & Arntz, 1993), social phobia (Hope et al, 1990; Becker et al, 2001), and patients with generalized anxiety disorder (Martin et al, 1991; Mogg et al., 1989; Bradley et al, 1995; Becker et al, 2001). Two competing explanations for the attentional biases observed in the emotional Stroop task are the general emotionality (positive or negative) theory vs. schema congruency or specificity theory. In their review, Williams, Mathews, and MacLeod (1996) conclude that the Stroop effect is not due to emotionality per se, but rather to the degree to which words are semantically related to the schema. Furthermore, comparing interference indices over a variety of studies, they find that although "current concern" accounts for much Stroop interference, it does not explain all the interference in patient groups. Besides schema- relatedness, the negativity of the material is also important. Becker et al.(2001) in their study found different attentional biases: patients with generalized anxiety disorder (GAD) were slowed by all types of emotional words, while patients with social phobia (SP) were distracted specifically by speech-related words. In the light of the pattern of findings the issue of how selective is the attentional bias in different anxiety disorders is still under scrutiny.

The present experiment sought to utilize the emotional-Stroop task to investigate the interaction of inhibitory processes in attention with threat-related stimuli. We have investigated these effects in two clinical populations: first in frontal lobe injured subjects, supposing that they have impaired inhibitional ability regardless of the emotional content of material; while in the GAD group we have supposed selective threat-related bias.

2. 5. 1. Method

2. 5. 1. 1. Participants

54 patients (aged between 23-60) were selected from the Neurology and Psychiatry Hospital and from the Rehabilitation Institute, Cluj- Napoca, Romania:14 with organic brain injuries affecting frontal lobes, 20 with clinically diagnosed Generalized Anxiety Disorder (GAD) and 20 control persons with no organic or psychiatric diseases. Table 2.6 presents the groups' characteristics.

Table 2.6. Demographical and neuropsychological characteristics of the groups

	Subjects with Frontal lesion (N = 14)	Subjects with GAD (N = 20)	Control subjects (N = 20)
Age (years)	49 (7.75)	49.45 (3.0)	45.15 (4.89)
Education (years)	12.12 (3.07)	12.62 (2.26)	12.69 (1.80)
Sex, male: female	6 : 8	6:14	12: 8
Lesion aetiology, TBI: AVM: cyste	2: 9: 3		

Note: Table values are mean (S.D.). Traumatic Brain Injury; AVM: Anterio-venous malformation.
The low and high anxiety groups differed significantly in state anxiety (M = 56.2, SD

The frontal lobe injured patients were identified by review of their medical records, consisting in computer tomography (CT) or magnetic resonance (MRI). Patients met the following inclusion criteria: presence of a single focal frontal lesion, at least 1.5 months time passed since onset. Specific details of lesions sites were not available and the medical notes indicated only laterality of injury and general extension. It should be noted, that patients were selected because their records indicated only frontal injuries, but it is, however, possible that minor lesions went undetected, and this is especially possible in the patients with closed head injuries. This could be a potential problem although it should be emphasized that their medical records indicated only frontal lobe pathology.

The potential GAD participants were given the "Structural Clinical Interview for DSM-III-R, UpJohn Version" (SCID-UP, Spitzer et al., 1987) by their clinical psychologist. Several potential participants were excluded due to medical illness, substance abuse and past or current psychotic episodes. The groups were equated with regard to age, gender, and level of education.

2. 5. 1. 2. Materials

State-Trait Anxiety Inventory (STAI-I., II)

All subjects completed the State-Trait Anxiety Inventory (STAI-I., II; Spielberger et al., 1970), but we have taken in consideration only GAD and control groups results. Using the romanian normative data (Lazar et al., personal communication) indicating in STAI-II. a mean score in trait anxiety level equal with 42. 11 (7.04) in women and in men equal with 40.78 (8.33), after excluding participants with near-median scores, we have selected in control group those with low trait anxiety score (M trait < 35) in order to minimise the proportion of the sample with mid-range levels of state anxiety at the time of testing. The GAD patients scored well beyond the average score (> 40) (M state score = 56.2; M trait score = 59.45), while the control group were selected only subjects with low state- and trait anxiety level (M state = 32.85; M trait = 33.2). The low and high anxiety groups differed significantly in state anxiety (M = 56.2, SD = 7.3, vs. M = 32.85, SD = 4.67, p < .01) and trait anxiety (M = 59.45, SD = 8.2, vs. M = 33.2, SD = 4.06, p < .01)

Pilot-study

The stimulus words used in experiments were selected and evaluated during a pilot study. A study list was prepared with 100 words, half of them supposingly threatening words and half of them supposingly neutral. All words were matched for lenght (2-4 syllabes) and frequency using norms on internet (www.szoszablya.hu). All words were rated by an independent group of 30 subjects on three dimension: anxiety-generating, excitement, and valence. After analysing of these ratings the most 30 and the less 30 threatening words were selected as stimulus material (see appendix).

Emotional Stroop task

Stimulus cards were used to present the words for the emotional Stroop task. Six A4 cards were prepared, each comprising 60 words, matched for word length and frequency. Each word was written in uppercase letters. One card consisted of rows of XXXXX (X. card), further card was the standard Stroop interference card: the words red, blue, green, yellow were written 60 times in random order, with each word written in a color that differed from the word itself (S. card). The second card pair consisted of a selection of 2 x 30 emotionally neutral words (e.g. clock, flower) written with black ink (RN Card) or colored red, blue, green or yellow in random order (CN card). The final pair consisted of 2 x 30 anxiety related words (e.g. blood, shame) written with black ink (RA Card) or colored red, blue, green or yellow (CA Card).

2. 5. 1. 3. Procedure

Participants were tested individually, lasting approximately 20 minutes. Each session had two phases: subjects first completed the STAI-I, II then they performed the emotional Stroop task.

In the Stroop task the subjects were instructed to read the words (RN and RA Cards) or name the color of the stimuli as quickly and as accurately as possible (S, X, CN, CA cards). The order of card presentation was determined randomly for each subject. The time spent on each of the stimulus was recorded and the mean time for each stimulus set was calculated.

Participants were debriefed at the end of the study.

2. 5. 2. Results and Discussion

A 3 x 6 two-way ANOVA was carried out with one between-subjects variable (groups) and one within –subjects variable (Stroop cards) using reaction time (RT) as dependent variable. A significant interaction effect was found, $F(2, 51) = 5.11$, $p = .001$. This analysis also revealed a significant main effect for group variable, $F(2, 51) = 5.98$, $p = .005$ and for Stroop conditions, $F(2, 51) = 2.12$, $p < .05$ (see Table 2. 7).

Table 2. 7. Comparison of global reaction times (sec.) in Emotional Stroop task

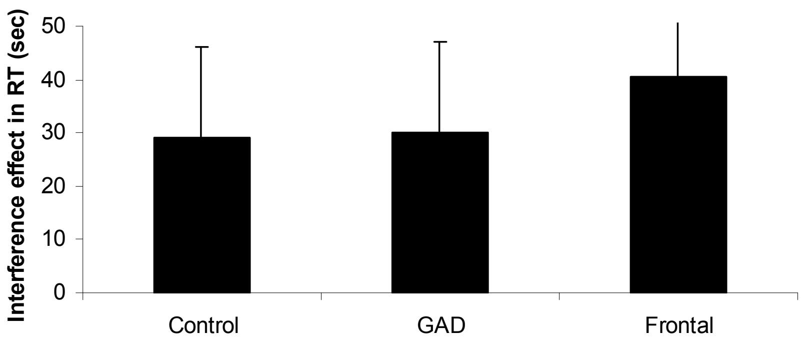
Emotional Stroop cards	Subjects with Frontal lesion (N = 14)	GAD group (N = 20)	Control group (N = 20)
RN	36.70 (12.70)	36.03 (20.86)	23.16 (15.21)
RA	38.24 (12.09)	37.41 (22.03)	25.79 (23.77)
X	39.22 (12.40)	31.23 (12.40)	23.15 (8.42)
S	79.63 (15.21)	61.13 (18.69)	52.01 (22.89)
CN	51.63 (13.69)	34.04 (10.62)	30.73 (8.45)
CA	51.76 (10.62)	41.77 (11.58)	34.04 (10.62)

Note: Table values are mean (S.D.). RN: reading neutral words; RA: reading annxiety-related words; X: color naming of X stimuli; S: standard Stroop intereference condition; CN: color naming of neutral words; CA: color naming of anxiety-related words

For further analysis we have compared the three groups with one-way ANOVA-s and independent t-tests. Significant differences were found in color naming of neutral words (CN) condition, $F(2, 51) = 6.38$, $p < .05$ and in color naming of anxiety-related words (CA) condition, F (2, 51) = 6.83, p <.01 Post-hoc Sheffe tests revealed that these differences are significant between frontal and GAD patients groups and between frontal and control groups, respectively. Comparing the performances of GAD and control groups significant differences were found in reading neutral words (RN) condition, t (38) = 2.28, p = .03, in naming the S card color, t (38) = 2.41, p =. 02, and in anxiety- related words contrasting (CA) condition, t (38) = 3.44, p ≤ .001

We have calculated two interference indices: the standard Stroop interference index, by subtracting RT for X card from RT for S-card and emotional Stroop interference index by subtracting RT for CN-RN cards from RT for CA-RA cards. Comparing the standard Stroop interference indices with one-way ANOVA, no significant differences were found, 1.73, p > .5 (see Fig. 2. 5a). The comparison of emotional Stroop interference index revealed a significant difference between groups, F (2, 51) = 9.97, p ≤ .001 (see Fig 2. 5b). Post-hoc Sheffe test revealed that this difference was due to the significantly stronger emotional interference effect in GAD group relative to the control and frontal lobe groups.

2.5.a



2.5.b

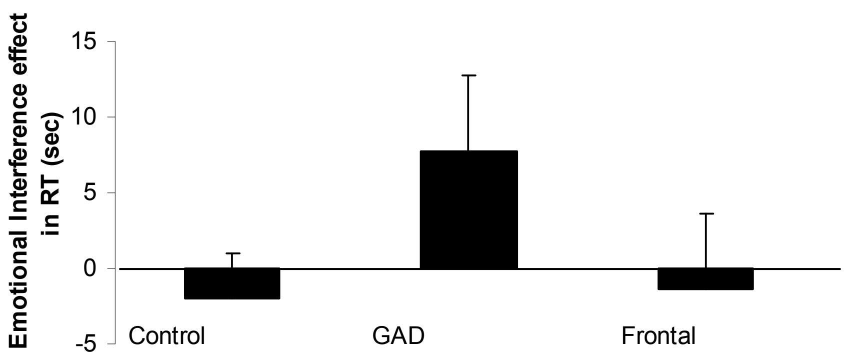


Figure 2. 5. Comparison of interference effect in emotional Stroop task. **2.5 a**. Standard interference effect (S – X); **2. 5 b.** Emotional interference effect: (CA-RA) – (CN – RN).

In summary, the data show that subjects with frontal lobe injuries have problems with both attentional inhibition, similarly to GAD patients, who exhibited difficulties only in identifying the color of anxiety-related words, even tought they were explicitly instructed to ignore the semantic content of the words. This finding is in line with previous studies demonstrating a general cognitive bias in frontal injuries and a selective bias towards the processing the threat-related stimuli in anxiety. The GAD and frontal patients not only have shown a significant interference effect, they were also somewhat slower in all conditions especially in reading neutral words and naming colours. This may be due to generally slowed information processing (but note that the control group was also formed from clinical population) in psychiatric and organic diseases. However in interference conditions a significant difference between groups was found only in interference conditions, demonstrating impaired inhibition in both groups.

2. 6. Emotional directed forgetting effect

While in the Stroop task naming the color requires automatic inhibition of the word's meaning, there are other paradigm involving intentional inhibition, such as the directed forgetting (DF) paradigm (Bjork, 1968; Woodward & Bjork, 1973; Bjork, 1989). The DF effect in non-clinical population was shown in a great number of studies (Bjork, 1989; Basden, Basden & Gargano, 1993; Johnson, 1994; Power et al, 2000; Albu, 2003; Payne & Corrigan, 2006), but under certain circumstances the inhibition ability can be impaired.

Studies investigating DF effect in clinical population, have shown impaired DF effect in TBI population (Schmitter-Edgecombe et al., 2004), especially with frontal lobe damage (Conway & Fthenaki, 2003; McDonald et al, 2006; Albu, Racsmany, & Conway, in press).

Few studies have examined intentional forgetting in the context of emotion, mainly concerning clinical disorders and coping styles. These studies have found no or diminished DF effect in depressed participants (Power et al, 2000), in schizophrenics (Racsmany et al, 2001; Racsmány et al., 2008), in obsessive-compulsive disorders (OCD), in post-traumatic stress disorders (PTSD) (Cloitre, 1992; Wilhelm et al, 1996; Cloitre et al., 1996; Cloitre, 1998), and in acute-stress disorder (ASD) (Moulds & Bryant, 2002; 2005). These studies demonstrated that the ability of intentional inhibition is impaired in anxious population and this impairment is more profound when the to-be forgotten information is threat-related. The issue of how selective this effect is in GAD patients remains, because no previous studies investigated the emotional selectivity of DF effect in this patient group.

Similarly to brain injured persons, the ability of intentional inhibition is impaired in anxious population, especially when the to-be forgotten information is threat-related. A number of studies tried to explore the neural basis of this selective bias in inhibiting emotional materials and the results emphasizing the role of amygdala and PFC, especially anterior cingulated cortex (ACG) in controlling emotional responses (LeDoux, 1995). Summarizing these data, it is likely that inhibitional inability of anxious subjects is due to the over-reaction of amygdala to the threat-related stimuli and to the disorder of ACG inhibitional control over the lateral amygdala nuclei (Braver et al., 2001).

The main aim of this experiment was to investigate the neural basis of inhibition and the interaction of inhibitory processes in memory with threat-related stimuli.These effects were investigated in two clinical populations: first in frontal lobe injured subjects, supposing that they have impaired inhibitional ability regardless of the emotional content of material; and in persons with generalized anxiety disorders (GAD). A novel feature of the study was that same subjects were tested on two measures of inhibitional bias, so that we could examine, within the same sample of participants, whether the use of different tasks may explain the findings noted above. Another question of the present experiment was the selectivity of inhibitional bias and the generality across tasks of this selective bias. We hypothesised that the selective bias toward threatening stimuli observed in the Stroop task can be observed in the DF paradigm as well, because automatic and intentional inhibition processes are executive functions and anxiety influences the whole executive system.

2. 6. 1. Method

2. 6. 1. 1. Participants

The 54 patients (14 with frontal lobe injury, 20 with GAD and 20 control subjects) who participated in study 2.5 took part in this experiment. All subjects completed the State-Trait Anxiety Inventory (STAI-I., II; Spielberger et al., 1970).

2. 6. 1. 2. Materials

Twenty-eight unrelated common words were selected from the pre-selected stimulus-material according to the following criteria: all words had 2-4 syllables, they were semantically unrelated and had approximately equal word frequency. Fourteen of the words were neutral and fourteen anxiety-related, and in the same list, no word started with the same letter. The anxiety related words were assigned to F list 1 and R list 1, while F list 2 and R list 2 contained the neutral words. Two study booklets were prepared with each word printed on a separate card in upper-case black letters. The first study booklet contained two sets of TBR words (seven words in each set) while the other study booklet contained a set of anxiety related TBF words (seven words) and a set of neutral TBR words (seven words). The two booklets were rotated across participants to counterbalance presentation order. A 2-minute paper and pencil arithmetic task was administered between the study phase and recall.

2. 6. 1. 3. Procedure

Participants were tested individually, lasting approximately 10 minutes. The DF procedure consisted of three phases: (a) study, (b) a filled interval, (c) free recall. In the study phase after the presentation of list 1 a remember (R cue) or a forgetting (F cue) was given, and then list 2 always with remember instruction. In the free oral recall test after two minutes filled interval, subjects were requested to try to remember the words previously seen in the study phase, regardless of which cue, R or F has been originally given. The recall test was terminated when the participant could not remember any more words, or when a 3-minutes interval had passed.

Participants were debriefed at the end of the study.

2. 6. 2. Results and Discussion

A 3 x 2 two-way ANOVA was carried out with groups as between-subjects variable and instruction type (R or F cue) as within –subject variable, using the recall rate as dependent variable. A significant interaction effect was found, $F(2, 51) = 27.29$, $p < .001$), and the main effect of instruction type was also significant, $F(2, 51) = 5.51$, $p < .05$) while the between subject effect was not significant, $F(2, 51) = .88$, $p > .5$).

For further analysis one-way ANOVA was used, showing significant effect of instruction type, $F(2, 51) = 4.40$, $p =.01$), due to the significantly higher recall rate of TBF items in GAD and frontal lobe groups. In the remembering control condition the control group recalled significantly more words, especially from the second list comparing with GAD and frontal lobe groups, $F(2, 51) = 7.48$, $p < .1$.

The two critical differences to show a DF effect are: reliable greater recall of and R list1 and F list 2 compared to F list 1. Analyzing separately the DF effect in groups, for the control group both critical comparisons were significant in the expected way, F1 - F2: $t(19) = 10.63$, $p \leq .001$; respectively F1 - R1: $t(19) = 9.29$, $p \leq .001$. This finding indicates a normal DF effect in control group. For the GAD group the first comparison was not significant, $t(19) = 1.87$, $p = .5$, while the second significant comparison, $t(19) = -2.78$, $p = .01$ suggest a rebound effect in which items targeted for inhibition are recalled to unexpectedly high level (see Table 2. 7 where the recall of F list 1 is significantly higher than the recall of F list 2). A similar pattern was found in the frontal lobe injured groups, where the two significant comparisons were not significant, F1 - F2: $t(13) = .26$, $p > 0.05$; and F1 - R1: $t(13) = .30$, $p > .05$, respectively.

Table 2. 8. Comparison of recalled words rate in emotional DF task

Groups	Forgetting condition		Remembering condition	
	F1 list	*F2 list*	*R1 list*	*R2 list*
Frontal lobe group (N = 14)	36.60(16.28)	35.71 (11.08)	49.28 (18.56)	41.26 (11.016)
GAD group (N = 20)	44.37 (15.42)	38.75 (19.42)	47.85 (16.88)	40.71 (11.61)
Control group (N = 20)	30 (14.04)	45.62 (11.48)	49.28 (16.30)	55.71 (15.30)

Note: Table values are mean (S.D). F: Forgetting condition; R: Remembering condition

Two inhibition indices were calculated: the standard DF inhibition index, by subtracting for each participant F list 1 from R List 1 and emotional DF inhibition index by subtracting for each participant F list 1 from F List 2 in the F-R free recall condition. Mean values equal with zero or lower indicate no inhibition. The standard DF inhibition index was compared with one-way ANOVA-s (see Fig. 2. 8) and a significant difference was found, $F(2, 51) = 12.26$, $p < .01$, with the GAD and frontal lobe injured groups showing significantly lower inhibition, than the control group. Comparing the emotional DF effect we found significant difference between groups $F(2, 51) = 27.79$, $p < .01$. Post-hoc Sheffe test revealed that only the control group showed inhibition, the GAD and frontal lobe groups had negative inhibition index.

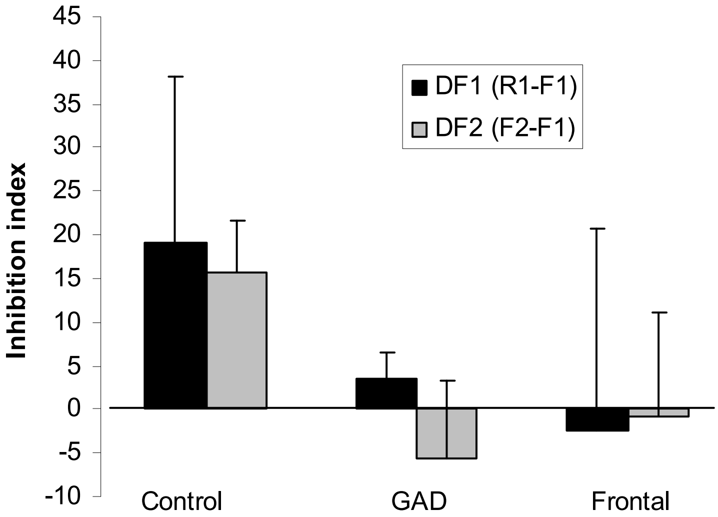


Figure 2. 6. Standard (DF1 = R1- F1) and emotional DF effects (DF2 = F2-F1)

This experiment indicates that patients with frontal lobe injuries and with GAD could not inhibit intentionally anxiety-related items designated as to-be-forgotten, in contrast a rebound effect was observed: they have recalled significantly more anxiety-related words despite the fact that these words were associated with forgetting-cued. On the other hand the control patients had normal DF effect. Thus from the present experiment it can be concluded that frontal lobe and GAD patients have intentional memory inhibition bias too, which in the GAD group is selective toward anxiety related stimuli.

2. 7. General Discussion

2. 7. 1. Inhibitory control and the right PFC

One of the aims of these studies was to investigate the role of the prefrontal cortex in inhibitory control processes using four widely used inhibitory paradigms: the Stroop task, the go/no-go task, the directed forgetting task and the selective retrieval practice task for retrieval induced forgetting effect. The findings of the first four inhibition experiments reported here point particularly strongly to a simple conclusion: patients with right frontal lobe injuries suffer impairments in intentionally initiating inhibitory processes. They do not, however, have similar impairments when inhibition is not intentional.

According to our results from Section 2.1, patients with right frontal lesion produced no inhibitory effect on the Stroop task, while the other patient group produced larger inhibitory effects compared to the right-frontal patients, although these effects in left frontal group were attenuated in comparison to the healthy control group. The impaired patients in each condition were also generally slower, but some frontal patients who did not make errors were also slow. Thus, it seems that time scores alone my not be the most effective measure of Stroop performance. The previous lesion studies that suggested left frontal regions as being most relevant for performance of the interference condition were based on the straight time-scores and did not control for direct color naming (see Peret, 1974; Golden; 1976). Left frontal lesions impaired direct color naming (Stuss et al., 2001; Stuss et al., 2002), complicating any interpretation of a Stroop effect. Slow color naming in the left frontal group was part of a generally slow response in all conditions in that group. In our study some of the patients with left frontal lobe lesions had increased errors and particularly slow performance in color naming, but even they did not show disproportionate interference in the incongruent condition. In Stuss et. al.'s study (2001), the first with control for baseline color naming and with precise lesion localization, demonstrated that the left lateral frontal effect is only for color naming directly, while exaggeration of the Stroop interference effect was observed in patients with bilateral or right side frontal lesion alone, similarly to our results, providing evidence for significantly greater Stroop interference effect in the right frontal group.

Results from Section 2. 2 provide similar evidence using the go/ no-go paradigm: patients with right frontal lesion showed no inhibitory effect, while other patient groups produced task-required inhibition. The right frontal group, due to the impaired inhibitory motor control, first produced false alarms and after a while, by learning the goal stimuli showed a higher RT. Given that the predominant form of injury in this group was closed head injury it seems likely that lesions would be widespread and diffuse, rather than focal, and this may have given rise to a general lowering of performance by networks in this region. However, it remains a question why this right frontal group exhibited more false alarms in no-go condition, producing also a bigger and statistically significant RT.

According to results from Section 2.3, patients with right frontal lesion produced a reversed inhibitory effect on the intentional forgetting task. Left-frontal patients produced larger inhibitory effects compared to the right-frontal patients, although these effects were attenuated in comparison to the healthy control group. Finally, the patient group with temporal lobe lesion produced a close to normal level of inhibition, while lateralization of the lesion size had no effect on the results. The analyses reported earlier established that patients with right frontal lesions showed the greatest degree of impairment with a reliable and abnormal tendency to recall more TBF than TBR items (Conway & Fthenaki, 2003). In contrast, patients with left frontal lesions were found to have a more normal pattern of performance. Their means were as predicted, and were the reverse of the right frontal group. A strong implication here is that networks in right frontal regions mediate willed attempts to forget recently acquired knowledge. The chief consequence of this is that executive processes cannot initiate effective (thought) avoidance under conditions of reduced processing resources, and therefore, paradoxically, TBF items become integrated with their representations in memory. Moreover, because available reduced resources become targeted on TBF rather than TBR items this leads to a better recall of the former relative to the latter – rebound effect (see Wegner, 1994, for review). Reduced processing resources in right frontal networks, the operations of which are attenuated by diffuse brain damage, prevent or disrupt thought avoidance and, consequently, inhibition is not triggered. The resources available are mainly used in the processing of TBR items. Ironically (see Wegner, 1994) this leads to the recall of more TBF than TBR items.

Altought our results support much of the research on directed forgetting in normal controls (Geiselman et al., 1983; Zacks et al., 1996), our findings are not entirely consistent with the limited research on directed forgetting that exists in patients with presumed frontal lobe damage (Andres & Van der Linden, 2002; Conway & Fthenaki, 2003; Schmitter- Edgecombe et al., 2004; McDonald et al., 2006). For example, nor Andres and Van der Linden (2002), nor Schmitter- Edgecombe et al. (2004) found impaired directed forgetting in patients with head injury relative to controls. Their patients, however, suffered from diffuse brain damage and there was no information provided as to the extent of their brain pathology. Conversely, Conway and Fthenaki (2003), similarly to our study, found that directed forgetting in free recall was abolished in patients with right frontal lobe damage and attenuated in patients with left frontal lobe damage relative to controls. McDonald et al. (2006) found the reverse pattern in their study in that the left frontal lobe group showed attenuated directed forgetting relative to the right frontal group. While the reasons for the discrepancies between our study and that of McDonald et al. (2006) are unclear, it could be related to differences in lesion location and/ or the nature of the tasks.

However, results from the Section 2.4 were somehow different: all of the patient groups, even the right frontal group, produced a normal level of retrieval induced forgetting, similarly to Conway and Fthenaki study (2003).

These striking dissociations between- and within- group have several implications. Most compellingly they suggest that the Stroop-task, go/ no-go taks, DF and RIF may involve different inhibitory processes or, alternatively, may involve different ways of initiating inhibition. We believe that the later is the case and that it is the way in which inhibition is triggered that differs. In the first three, inhibitions are intentionally triggered, involving active thought avoidance, while in the RIF inhibition occurs automatically and does not require any intentional thought.

The main conclusion to be drawn from the data is that the right frontal cortex has a fundamental role in intentional inhibitory processes, according to the inhibitory theory of Aaron et al. (2004), pointing to the right inferior frontal cortex as the center of the inhibitory executive system.

It should be also noted that the neuropsychological study of executive functions could benefit from a better input from cognitive science before it can provide a consistent feedback. This is particularly the case with inhibition, a concept that refers to several different processes and with low construct validity (Rabbitt et al., 2001). In this domain for example, there is a strong evidence for a nonunitary nature (Arbuthnott, 1995; Connely & Hasher, 1993; Popp & Kipp, 1998; Racsmany et al., 2008). Given that the term is commonly used to describe a wide variety of functions at a number of levels of complexity, it would be necessary to determine what cognitive factors might distinguish between different inhibitory mechanisms. The existing evidence suggest that the level of attentional control is crucial, for example (Arbuthnott, 1995), and that not all inhibition tasks are executive in nature. In this perspective, some inhibitory tasks (e.g. retrieval inhibition, negative priming or inhibition of return) involve inhibition processes that occur without the awareness of the participant. Our results provide evidence that the effects of frontal lesions is greater in tasks requiring deliberate, intentional or controlled inhibition as compared to task requiring automation or unintentional inhibition.

2. 7. 2. Anxiety related inhibition impairment

The second aim of this study was to investigate the selectivity of inhibitional bias and the generality of this selective bias in anxiety disorders. The results are in line with previous studies, indicating a lower inhibitional ability in frontal lobe and in anxious people. The frontal lobe injured persons showed a general interference effect in the emotional Stroop- task regardless of the emotional value of stimuli, they were slow in naming color of color names (standard Stroop – condition) for neutral and threatening words too. Persons with GAD showed a selective interference effect toward threat-related stimuli in the emotional Stroop- task. Despite the fact that the GAD group was generally slower in all interference conditions and they produced more errors these differences were significant only in threat-related interference condition. This finding is in accordance with Eysenck's (1991) theory postulating that the attention focus of anxious persons is more easily distractible probably because they perceive all kind of stimuli like possible danger, requiring an extra processing effort for threatening stimuli. MacLeod & Matthews (1988; Matthews & MacLeod, 1994) propose that threat-related material shows an enhanced ability to capture the selective system in anxious individuals, and previous research on selective attention shows that emotional stimuli capture attention quickly and involuntary. The present study offers support for this hypothesis, suggesting that anxiety-prone individuals have rather undifferentiated cognitive representations of threat (danger schemata) that are easily activated by the presence of danger-relevant cues, resulting in a selective allocation of processing resources toward such information (Beck & Clark; 1991).

In the DF task no directed forgetting effect was found in the GAD and frontal lobe groups, while in the clinical control group the DF effect was normal. In the forgetting condition GAD and frontal lobe injured persons recalled significantly more words from the first to-be-forgotten list, than control subjects, who have recalled significantly more words from the second to-be-remembered list. In the remembering condition the results were different from the forgetting condition: the control subjects have recalled significantly more words from both the first and the second list, compared with GAD and frontal lobe groups. Results also indicate that the two clinical groups could not intentionally forget the emotionally valent, previously learned material. These results are in accordance with some previous studies showing no directed forgetting effect in clinical population (Wilhelm, McNally, Baer & Florin, 1996; Cloitre, 1998; Conway & Fthenaki, 2003; McDonald et al., 2006), suggesting that affective experience undermines forgetting but they do not identify mechanisms for the effect. The retrieval-inhibition theory of intentional forgetting outlines two critical processes (Bjork, 1989). The first is the mental segregation of to-be-forgotten items from to-be remembered items. The second process is retrieval inhibition, intentionally reducing activation for memory items (Anderson & Bjork, 1994). Intentionally forgotten events are not erased from memory, but access to them is blocked. Emotions might intervene at either steps. Because emotional items are processed more elaborately than neutral items, participants might form more link between emotional items and other memories, in concordance with Bower's (1981) emotional network theory, this way reducing the segregation between to-be-forgotten and to-be remembered items. Emotion may also interfere with retrieval inhibition because emotion renders events salient, and therefore highly accessible (Payne & Corrigan, 2006).

An another interesting finding was that GAD and frontal lobe injured persons generally showed a lower recall rate both in forgetting and in remembering conditions. This can be explained with a possible smaller working memory capacity in frontal lobe injured persons and in GAD subjects too, but in the latter case, possibly due to the extra processing resources required by threat-related stimuli (West, 1999), resulting also in a selective goal-neglect process (Duncan, 1993; Duncan et al, 1996). The goal-neglect phenomenon first was described in frontal lobe injured persons, who had difficulties in the selection of appropiate goals. In addition to a generalized interference effect in frontal lobe injured subjects we found an intentional inhibitional impairment too, resulting in reverse directed forgetting effect, which can be explained by difficulties in inhibiting irrelevant information and by difficulties in selective activation of relevant information (Kingma et al, 1996).

In our study GAD patients recalled more threatening to-be-forgotten words suggesting that in addition to emotionally selective bias in the GAD group, an effect that Wegner (1989, 1994) referred to as "ironic mental" control, must also be considered. These phenomena suggest the possibility of a common mechanism in which the attempts to inhibit threat- or aversive personally relevant information lead to a greater facilitation of intrusions into consciousness. This effect may also possibly explain some of the intrusive phenomena that are seen in post-traumatic stress disorder in which attempts to avoid distressing thoughts related to trauma often seem to lead to more rather than less experience of the intrusions (e.g. Power & Dalgleish, 1997; Power et al., 2000).

Given its potential clinical relevance, intentional forgetting has been suggested as one way that people may replace troubling memories with happier ones (Bjork, Bjork & Anderson, 1998). Our findings contribute to the question of whether forgetting can be helpful in some situations (e.g. coping with traumatic experiences); though caution is needed in generalizing from the mild emotions of the laboratory to the intense emotion that can characterize the real life (e.g. trauma). These comments are of course speculative, but they suggest interesting further exploration of these phenomena. Theories that include intentional forgetting of emotional memories may need to specify how this forgetting is accomplished and how a coping strategy manages to overcome the basic advantages that emotional events have in attention and memory.

The results of this study show that while the emotional Stroop-task is suitable for examining emotionally selective bias in attention processes, the directed forgetting task is an ideal one to extend both the investigation of the interaction of cognition and emotion and for examining the inhibitory effects in normal and in different clinical populations. The similar findings and the correlation between automatic and intentional inhibition tasks indicates that emotion may interfere at a higher level with the cognitive processes. Since automatic and intentional inhibition processes are considered as sub-processes of executive system it seems plausible that anxiety may interfere with the whole executive system. A number of questions remain to be answered by future experiments. For example, are the effects shown by GAD patients in this study due to wider anxiety schemata? What kind of material is most specific for individual anxiety disorders? Can these selective biases toward threatening material be observed in other experimental and clinical tasks depending on executive system functioning?

Whatever the answers to these questions will be, experimental paradigms derived from cognitive psychology such as Stroop task and DF paradigm will be helpful in investigating the interaction of cognitive and emotional processes. This is an especially important issue, because the effectiveness of a cognitive system depends not only from the maintenance and organization of relevant informations, but also on succesfull inhibition of irrelevant information. Negative emotions, like anxiety can have negative effect by disturbing the effectiveness of the executive system, causing pseudoexecutive symptoms even in people without organic defficits, or can alter non-executive neurological symptoms in brain injuried persons. Persons who suffered a brain-injury have to deal with negative emotions, especially anxiety, and this can alter the clinical syndrome. From differential diagnostic perspective it is especially important to be able to separate somehow the real dysexecutive symptoms from pseudo-dysexecutive symptoms caused by negative emotions. In the following sections we tried to control the emotions-caused pseudo-dyexecutive symptoms, by using clinical control groups with aproximatley the same anxiety level as the examined brain injured groups.

3. The role of lateralized executive functions in memory retrieval

Most theories of lateralization posit some combination of material-specificity and process-specificity, but the amount of these factors and their interaction are still not clear. Lateralized executive functions of the two hemispheres in memory retrieval are explained by different theoretical models in different ways: one explanation relies e.g. on evidence of material specifity provided by classical neuropsychological studies , another explication is given by Tulving's well known hemispheric encoding/ retrieval asymmetry (HERA) model (Tulving, Kapur, Craik, Moscovitch, & Houle, 1994), or recently developed new hypothesis, like the "cortical asymmetry of reflective activity" (CARA) model (Nolde, Johnson, & Raye, 1998b) and "production-monitoring" hypothesis (Cabeza, Locantore, & Anderson, 2003).

3. 1. Theoretical models of lateralized memory retrieval

3. 1. 1. Classical neuropsychological view for material-specificity

The material-specific model asserts that memory function lateralizes with language function: in left-language dominant individuals, the left hemisphere mediates verbal information processing, whereas the right hemisphere is more involved in visual processing (P. Milner, 1974). The model is supported by numerous studies of temporal lobe epilepsy (TLE) patients who experienced selective memory deficits following unilateral resection of the epileptogenic medial temporal lobe (MTL). Removal of the left hippocampus and surrounding structures consistently produces verbal memory deficits and, although the findings are less robust, removal of the right hippocampal complex has resulted in memory deficits for non-verbal materials including mazes, unfamiliar faces, abstract patterns, and melodies (B. Milner 1968; Jones-Gotman, 1986; Zatorre & Samson, 1991; Plenger et al., 1996; Kelley et al., 1998; Golby et al., 2001). This model has been extended to characterize lesion-deficit patterns in the frontal lobes. Unilateral frontal lobe lesions can produce material-specific deficits (Whitehouse, 1981; B. Milner, 1982; Wagner et al., 1998; Mc Dermott, Buckner, Peterson, Kelley, & Sanders, 1999; Golby et al., 2001; Kelley et al., 2002), but such deficits are not always found. Furthermore, frontal lesions tend to produce milder deficits, sparing recognition memory but impairing free recall, new episodic memory formation, and context-sensitive retrieval processes (Shimamura, 1995; Lee, Robbins, Pickard, & Owen, 2000a; Kelley et al., 2002). Functional neuroimaging studies have shown that left prefrontal activation correlates with the verbalizability of nonverbal stimuli, and right lateral prefrontal regions with the imageability of verbal stimuli. Furthermore, the results provided preliminary support for an alternative hypothesis: the apparent asymmetry within episodic memory may reflect the differential involvement of verbal and non-verbal processing mechanisms during encoding and retrieval (Lee, Robbins, & Owen, 2000b). These results called into question whether material-specificity findings can account for neuroimaging results and the extent to which hemispheric specialization in the MTL and PFC depends on the external characteristics of a stimulus or are influenced by internally generated stimulus representations and memory processes.

3. 1. 2. HERA model

Tulving, Kapur, Craik, Moscovitch, and Houle (1994) have proposed a process-specific alternative explanation: the hemispheric encoding/retrieval asymmetry (HERA) model. According to HERA, the left PFC is more involved in encoding processes than the right PFC (specifically semantic retrieval), whereas the right PFC is more involved in episodic memory retrieval than the left PFC (Tulving et al., 1994; Habib, Nyberg & Tulving, 2003). HERA is supported by large amounts of data that consistently show that left PFC is biased for encoding verbal materials (Tulving et al., 1994; Shallice et al, 1994; Nyberg, Cabeza, & Tulving, 1996a; Nyberg et al., 1996b; Iidaka, Sadato, Yamada, & Yonekura, 2000) and non-verbal materials (Haxby et al., 1996; Owen, Evans, Petrides et al., 1996; Buckner et al., 1998; Nyberg et al., 2000; Iidaka et al., 2000; Johnson, Raye, Mitchell, Greene, & Anderson, 2003), whereas the right PFC is biased for the retrieval of verbal materials (Shallice et al., 1994; Nyberg et al., 1996a; Nyberg et al., 1996b; Cabeza & Nyberg, 2000; Lepage, Gaffar, Nyberg, & Tulving, 2000; Fletcher & Henson, 2001) and non-verbal materials (Mc Dermott et al., 1998; Nyberg et al., 2000; Grady, McIntosh, Beig, & Craik, 2001; Johnson et al., 2003). Gazzaniga (2000) has observed a cerebral specialization in mnemonic functions in which the left hemisphere is more specialized for semantic processing and the right hemisphere for episodic memory. It is known that episodic encoding relies heavily on semantic processes; therefore, it is reasonable to consider that left lateralization of encoding is attributable to the semantic processing of information to-be-memorized. The right lateralization of episodic retrieval has been accounted for in terms of 'retrieval mode' (Lepage et al., 2000). Retrieval mode refers to a neurocognitive set, a necessary condition that sets the stage for episodic remembering. This hypothesis provides a plausible explanation for the frequently observed left lateralization of retrieval under conditions in which retrieval mode is held constant (Henson, Shallice, & Dolan, 1999; Henson, Rugg, Shallice, & Dolan, 2000; Rugg, Henson, & Robb, 2003). During episodic retrieval, the right frontal activity has been hypothesized to reflect not only a retrieval mode, but also a retrieval effort (Brewer, Zhao, Desmond, Glover, & Gabrieli, 1998; Kirchhoff, Wagner, Maril, & Stern, 2000) and the retrieval success (Wagner et al., 1998; Lee et al., 2000b) or post-retrieval evaluation processes (Lee et al., 2000a; Nyberg et al., 2000). Furthermore, using latent variables analysis, Nyberg et al. (2003) demonstrated that material-specificity can occur independently of process-specificity.

3. 1. 3. CARA model

The CARA model was developed by Nolde et al. (1998b) and proposed a new hypothesis to explain previous findings showing increased left PFC activity during episodic memory tests (Swick & Knight, 1996; Nolde, Johnson & D'Esposito). The CARA model assumes that the right PFC is more involved in a variety of heuristic component processes that are sufficient for relatively simple episodic memory tasks but that more complex episodic memory tasks require additional systematic component processes mediated by the left PFC. Several pieces of evidence have emphasized that the left PFC might have a role in episodic retrieval, especially in tasks demanding more systematic component processes, such as autobiographical recall (Johnson et al., 1997), word-stem cued recall (Swick & Knight, 1996; Nolde et al., 1998b), source memory, and context recognition tasks (Johnson, Kounios & Reeder, 1994; Johnson, Kounios & Nolde, 1996; Nyberg et al., 1996).

This pattern suggests a "systematic – heuristic" hypothesis, stating that the right PFC might be able to refresh activated information, shift between representations, and note relations, components of many heuristic processes. In contrast, the left PFC might be recruited for more systematic processes, including rehearsing, more detailed, deliberative analysis of activated information, initiating strategies, and generating cues for retrieving inactive information (Nolde et al., 1998a). The CARA hypothesis also suggests that the association of the right PFC with retrieval and the left PFC with encoding, as suggested by the HERA model (Tulving et al., 1994), might reflect a difference in the processing requirements of the retrieval and encoding tasks that have been compared (Nolde et al., 1998b). Consistent with the systematic-heuristic hypothesis, a meta-analysis of PFC activations in PET/ fMRI studies of episodic retrieval showed that PFC activations tend to be right-lateralized for tasks classified as heuristic but bilateral for tasks classified as systematic (Nolde et al., 1998b).

3. 1. 4. The production-monitoring hypothesis

Previous lesion and functional neuroimaging studies have demonstrated the role of the left PFC in semantic retrieval (for reviews, see Gabrieli, Poldrack & Desmond, 1998; Cabeza & Nyberg, 2000), whereas the role of the left PFC during episodic retrieval has been primarily attributed to semantic and generation operations (Nyberg et al., 1996a; Cabeza, Rao, Wagner, Mayer, & Schacter, 2001). In contrast, the role of the right PFC during episodic retrieval has been attributed to verification and checking operations (Schacter, Curran, Gallucio, Milberg, & Bates, 1996; Rugg, Fletcher, Chua, & Dolan, 1999; Fletcher, Shallice, Frith, Frackowiak, & Dolan, 1998; Cabeza et al., 2003). The 'production-monitoring' hypothesis (Cabeza et al., 2003), based on these findings, proposes that during verbal episodic retrieval, the left PFC is differentially more involved in semantically guided information production processes, whereas the right PFC is differentially more involved in monitoring and verification processes. This model assumes that production processes play a more important role in recall than in recognition tests, whereas monitoring processes play a more important role in recognition than in recall tests (Kintsch, 1968; Anderson & Bower, 1972; Cabeza et al., 2003). These studies also provided evidence for various amounts of production and monitoring operations among different recognition and recall tasks. Cabeza et al.'s model assumes, for example, that associative-recall and context-recognition tasks involve a greater amount of production processes than item-recognition tasks. Since context-recognition tasks involve the production of contextual information and demanding monitoring operations, they are likely to involve a greater amount of production and monitoring components than simple item-recognition tasks, according to the CARA hypothesis of Nolde et al. (1998b). This idea is supported by the evidence provided by functional neuroimaging studies showing a bilateral PFC activation during context recognition (Cabeza et al., 1997; Rugg et al, 1999; Raye, Johnson, Mitchell, & Nolde, 2000; Dobbins, Foley, Schacter, & Wagner, 2002; Lundstrom et al., 2003), which may be related to increased demands on systematic retrieval control operations (Nolde et al., 1998a; Johnson & Raye, 2000; Cabeza et al., 2003) including monitoring (Henson, Homberger, & Rugg, 2005) and cue specification processes (Fletcher et al., 1998) during source judgments, all of which depend on inhibitory and/or selection mechanisms (Cabeza et al., 2003). On the other hand, in contrast to the CARA model, the production-monitoring hypothesis suggests that some tests classified as systematic could have involved a greater production component (for example, stem-cued recall task) and those classified as heuristic, a greater monitoring component (such as the item-recognition task). Cabeza and colleagues (2003), in order to compare these two latter hypotheses, have crossed the systematic-heuristic and production-monitoring factors by selecting tasks that involve more systematic and monitoring processes (e.g., context-recognition task) and a task that involves more heuristic and production processes (e.g., associative-cued recall), respectively. By contrasting this hypothesis directly within subjects and under similar experimental conditions, Cabeza et al. (2003) provided evidence for the production-monitoring hypothesis in an fMRI study. The results sustained another assumption of their model, proposing that production and monitoring processes may occur regardless of whether the level of memory recovery is high or low. Finally, they found a shift from the left PFC to the right PFC during retrieval processes, suggesting that production processes primarily occurred during early (''prerecovery'') and intermediate (''recovery'') phases of retrieval, whereas monitoring processes primarily occurred during intermediate and late (''postrecovery'') phases of episodic retrieval (Allan & Rugg, 1997; Donaldson & Rugg, 1999; Conway, Pleydell-Pearce, & Whitecross, 2000; Cabeza et al., 2003).

3. 2. The rationale of the study

The main purpose of the present lesion study was to examine the role of the two hemispheres in the different executive and memory processes during episodic memory retrieval. Specifically, we aimed to contrast the lateralization hypothesis presented above, using Cabeza's original contrasting method (see Cabeza et al., 2003) and adding the verbal-visual factors and Tulving and colleagues' encoding-retrieval factors. Ten episodic retrieval tasks were used: verbal and visual associative cued-recall (ACR), verbal and visual stem cued-recall (SCR), verbal and visual item recognition (IRN), verbal and visual context recognition (CRN), and context cued recall (CCR). As illustrated in Figure 1, the 10 episodic memory tests fill the cells of a 3 x 3 matrix, crossing production-monitoring, systematic–heuristic, and verbal-visual factors. As noted above, recall tasks (SCR, ACR, CCR) can be assumed to involve a greater production component than recognition tasks, and recognition tasks (CRN and IRN) to involve a greater monitoring component than recall tasks. At the same time, these tasks can be organized along the systematic–heuristic dimension on the basis of criteria proposed by Nolde et al. (1998b). The categorization of memory tasks proposed by Nolde is similar to the suggestions of Tulving and colleagues' HERA model (Habib et al., 2003). From this point of view, the ACR tasks can be categorized as memory tasks involving more encoding processes, whereas SCR, CRN, and CCR tasks are more dependent on retrieval processes. As indicated by the headings in Figure 3.1, these task classifications are relative, not absolute. For example, IRN is less systematic than CRN, but it may be more systematic than forced-choice recognition (Nolde et al., 1998b). The relativity of task classifications is not a problem in the current study because the predictions investigated are also relative. The fact that the matrix in Figure 1 classifies tasks as having more production or more monitoring processes does not indicate that these two types of processes are always inversely related. Production and monitoring are not the endpoints of a single continuum, but two different continua, and it is possible to develop tasks that are high in both or low in both types of processes. This assumption is also true for the systematic-heuristic and encoding-retrieval factors.

Factors	**Production processes**	**Monitoring processes**	
Systematic processes	Verbal Stem Cued-Recall (SCR)	Verbal Context Recall (CCR)	Verbal Context Recognition (CRN)
	Visual Stem Cued-Recall (SCR)	Visual Context Recall (CCR)	Visual Context Recognition (CRN)
Heuristic processes	Verbal Associative Cued-Recall (ACR)	Verbal Item Recognition (IRN)	
	Visual Associative Cued-Recall (ACR)	Visual Item Recognition (IRN)	

Figure 3.1. Factorial design contrasting Verbal - Visual, Production - Monitoring and Systematic - Heuristic factors

3. 3. Method

3. 3. 1. Participants

Forty patients participated in this study: 10 patients with right frontal lobe lesions, 10 patients with left frontal lobe injuries, 10 with left temporal lobe lesions, 10 with right temporal lobe lesions. The patients were recruited from the National Institute for Medical Rehabilitation, Head-and Brain Injury Department and from the National Institute of Psychiatry and Neurology, Epilepsy Department, in Budapest, Hungary. Subjects older than 65 years, with a native tongue other than Hungarian, or with a history of psychiatric or other neurological disease were excluded. Patients were selected upon a review of their medical records including computer tomography (CT) or magnetic resonance imagery (MRI). Patients met the following inclusion criteria: presence of a single focal unilateral frontal or temporal lesion and time since onset greater than 1.5 months. Specific details of lesion sites were not available and the medical notes indicated only laterality of injury and general extension. It should be noted that patients were selected because their records indicated only frontal or temporal injuries. However, it is possible that minor lesions went undetected, and this is especially possible in the patients with closed head injuries. This could be a potential problem; however, it must be emphasized that their medical records indicated only frontal or temporal lobe pathology.

Table 3. 1 presents the patients' characteristics. The right frontal patients averaged 35.05 years of age (range 17-60) and 11.36 years of education (range 8-17 years); the left frontal group had an average age of 37.72 years (range 16-60) and 12.63 years of education (range 8-17). The mean age and educational level for the right and left temporal group were 30.1 years of age (range 16-45) and 13.2 years of education (range 8-16) and 31.3 years of age (range 16-48) and 11.1 years of education (range 8-16), respectively.

Subjects with frontal and temporal cortex lesions were compared with 10 matched control subjects. This clinical control group was composed of matched patients from the National Institute for Medical Rehabilitation, Spinal Cord Injury Department with the same characteristics as the patient groups, but without a history of neurological or psychiatric disorder. Our reason for using clinical controls instead of healthy ones was that the clinical environment (i.e., the "patient" role), which may influence anxiety factors, was similar for all groups examined. The 10 control subjects (7 male and 3 female) were matched approximately with the patients based on age, education, and IQ. Their average age was 32.6 years (range 17-56) and time spent in education was 12.6 (range 8-17 years).

After providing a complete description of the study to the subjects, informed written consent was obtained. The Ethical Committee of the National Institute for Medical Rehabilitation, Budapest approved the study design.

Table 3. 1. Demographic and clinical characteristics of all subjects

	Right Frontal lesion group (N = 10)	Left Frontal lesion group (N = 10)	Right Temporal lesion group (N = 10)	Left Temporal lesion group (N = 10)	Clinical control group (N = 10)
Age (years)	35.09 (16.11)	32.72 (13.77)	30.10 (9.32)	31.30 (9.58)	32.60 (13.72)
Education (years)	11.36 (2.76)	12.63 (2.54)	13.20 (2.52)	11.10 (.56)	12.60 (3.16)
Sex, male: female	6 : 4	9 : 1	6 : 4	4 : 6	7 : 3
Lesion aetiology, TBI: EP:HSE	10: 0: 0	10 : 0: 0	7 : 2 : 1	4 : 6 : 0	

Note: Table values are mean (S.D.). TBI: Traumatic Brain Injury; EP: Epilepsy; HSE: Herpex Simplex Enchephalitis

3. 3. 2. Episodic memory tasks

Ten episodic retrieval tasks (Fig. 3. 2) were used: verbal and visual associative cued-recall (ACR), verbal and visual stem cued-recall (SCR), verbal and visual item recognition (IRN), verbal and visual context recognition (CRN) and recall (CCR). Each task consisted of 8 items or 8 pairs of items. In the ACR condition, the patients studied unrelated word pairs or simple drawings pairs. At test, they were presented with the first word or drawing of each pair and were asked to recall the second word or drawing. In the SCR condition, subjects studied single words or simple pictures, and at test, they recalled a studied word or picture that fitted word stems or picture stems. The IRN condition was a standard old/new recognition paradigm with remember/know judgments using eight similar distractors in the recognition phase. In the study phase of the verbal CRN condition, half of the words were presented with a female and half with a male voice, and at test, probe words were classified as ‘‘female voice’’ or ‘‘male voice’’. In the visual CRN condition, half of the pictures were presented with white background and half with black background. In the test phase, the subjects determined whether a picture was previously presented with white or black background. Finally, the CCR condition was a standard source memory task in which half of the words or pictures were presented in List 1 and half, a little later, in List 2. In the test phase, the subjects categorized the words or pictures as part of one of the two lists (List 1 or List 2).

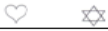
Tasks	Study Stimuli	Test Stimuli	Test Responses
1.Verbal ACR	Family- Material	Family	Material
2.Visual ACR			
3.Verbal SCR	Window	Win____	Window
4. Visual SCR			
5.Verbal IRN	Medic	Medic Doctor	Studied/ New Remember/ Know Studied/ New Remember/ Know
6. Visual IRN			Studied/ New Remember/ Know Studied/ New Remember/ Know
7. Verbal CRN 8. Verbal CCR	Program	Program	Male/Female List1/List2
9. Visual CRN 10. Visual CCR			Background Same/New List1/List2

Fig. 3. 2. Experimental episodic memory tasks. ACR: Associative-cued recall; SCR: Stem-cued recall; CRN: Context recognition; CCR: Context-cued recall; IRN: Item recognition

3. 3. 3. Procedure

Each patient was tested individually in two sessions (each session lasted approximately 1.5-2 hours). The order of episodic memory tasks and executive tasks was random for each patient. Between the encoding and retrieval phases of episodic memory tasks, 2 minute-long arithmetic tasks were used as distractors. Participants were tested either at the National Institute for Medical Rehabilitation or at the National Institute of Psychiatry and Neurology, Epilepsy Department, Budapest. Consent to participate was obtained after full disclosure of the study's purpose, risks, and potential benefits. At the conclusion of the study, all participants were debriefed and provided an opportunity to ask questions regarding the study.

3. 4. Results

3. 4. 1. Standardization results

Given the possible differences in difficulty between the 10 episodic memory tasks, a standardization pilot study was performed with 33 (18 male/15 female) healthy control subjects aged 17-52 (Mean age = 25.69). The mean score of the experimental episodic memory tasks was calculated (M = 5.64) and from this mean score, we calculated the standardization indices for each task. The standardization indices for each task in order of difficulty are as follows: CCR visual = .82; CCR verbal = .91; SCR visual = .91; ACR visual = .94; SCR verbal = .95; IRN visual = .97; ACR verbal = .98; CRN verbal = .99; IRN verbal = 1.11; CRN visual = 1.25.

In the subsequent statistical analysis, we used the standardized score of each task (raw scores * standardization index).

3. 4. 3. Lateralization group results

3. 4. 3. 1. Between-Group Comparisons

In order to examine the differences in task type across the groups, one-way ANOVA was conducted. We found significant differences between groups in: SCR visual (F (4, 45) = 3.33, $p < .01$), CRN verbal (F (4, 45) = 2.80, $p < .05$), CRN visual (F (4, 45) = 3.11, $p < .05$), and CCR visual conditions (F (4, 45) = 2.57, $p = .05$). In the other conditions, ACR verbal (F (4, 45) = 1.35, $p > .05$), ACR visual (F (4, 45) = 2.39, $p > .05$), IRN verbal (F (4, 45) = .63, $p > .05$), IRN visual (F (4, 45) = .81, $p > .05$), SCR verbal (F (4, 45) = .80, $p > .05$), and CCR verbal conditions (F (4, 45) = 1.49, $p > .05$), the differences were not significant. Post-hoc Sheffe tests revealed significant differences in SCR visual condition between the left temporal group and the clinical control group. In CRN verbal condition, the left temporal group displayed the poorest performance, whereas in CRN visual condition, the right frontal and right temporal groups exhibited the most affected performances relative to control and left frontal groups. In CCR verbal condition, the two temporal groups had the poorest recall rates, whereas in CCR visual condition, all of the patient groups were affected in comparison with the control group (see Table 3. 2).

Next, we separately examined the Remember/Know responses in the two IRN tasks. One-way ANOVA revealed a significant difference only in IRN visual condition Know responses, F (4, 45) = 2.72, $p < .05$, due to the left temporal group providing more Know responses than the other groups. In the other conditions, no significant differences were found.

In order to examine the interaction between task types and groups, we conducted a 2 x 5 x 5 mixed factorial design with Task modality (verbal/ visual) and Retrieval condition (ACR/ SCR/ IRN/ CRN / CCR) as within-subjects factors and Group (right frontal/ left frontal/ right temporal/ left temporal/ control) as a between-subjects factor. The dependent variable was the standardized score of each task. The interaction of these three factors was not significant, F (16,

4) = 1.44, *p* > .05. The interaction effect between Task modality and Groups was significant, *F* (4, 4) = 3.51, *p* < .05, but the interaction between Retrieval condition and Group was not significant, *F* (16, 4) = .78, *p* > .05. The main effect of Retrieval condition showed a strong significance, *F* (4, 4) = 8.58, *p* < .001, as did the main effect of the task type, *F* (1, 4) = 10.36, *p* < .005. The main effect of the between-subject factor showed only a slight tendency toward significance, *F* (16, 4) = 1.44, *p* = .1.

3. 4. 3. 2. Within-Group Comparisons

In order to examine how the task-type affects recognition and recall performances within each of the groups, five repeated measure ANOVAs were conducted separately for each group.

Table 3. 2. Groups performances on the 10 episodic memory tasks

	Right Frontal lesion group (N = 10)	Left Frontal Lesion group (N = 10)	Right Temporal lesion group (N = 10)	Left Temporal lesion group (N = 10)	Clinical control group (N = 10)
ACR verbal	4.4 (2.58)	2.89 (2.70)	3.87 (2.24)	2.84 (1.61)	4.50 (1.64)
ACR visual	2.86 (1.40)	3.37 (1.99)	2.35 (1.77)	3.66 (2.20)	4.88 (2.37)
SCR verbal	5.30 (2.11)	5.20 (1.92)	5.84 (1.91)	4.25 (1.94)	5.52 (2.57)
SCR visual	4.60 (1.38)	5.20 (1.68)	5.23 (1.39)	3.55 (1.40)	5.50 (.72)
CRN verbal	5.30 (1.10)	6.20 (1.25)	5.54 (1.16)	4.45 1.56)	6.04 (1.5)
CRN visual	5.70 (1.59)	8.25 (1.12)	5.42 (1.29)	6.87 (1.16)	5.60 (2.31)
CCR verbal	5.00(1.73)	5.46 (1.66)	4.18 (1.22)	4.26 (1.10)	5.57 (.76)
CCR visual	4.68 (1.03)	4.75 (1.77)	4.51 (1.35)	4.70 (1.14)	6.10 (.44)
IRN verbal	5.45 (1.75)	5.00 (2.63)	5.00 (1.90)	4.21 (2.01)	5.33 (2.50)
IRN visual	4.80 (1.68)	5.30 (1.64)	5.33 (1.53)	5.43 (1.30)	6.20 (1.66)
IRN verbal R	4.23 (1.38)	4.41 (1.00)	4.32 (1.81)	4.37 (1.62)	4.61 (.85)
IRN verbal K	.99 (.97)	.90 (.63)	.63 (.78)	.72 (.59)	.97 (.91)
IRN visual R	5.44 (.73)	4.30 (.69)	4.91 (1.66)	4.58 (1.04)	5.53 (.83)
IRN visual K	.26 (.39)	.87 (.73)	.53 (.88)	1.10 (.85)	.24 (.38)

Note: Table values are mean (S.D.). ACR: Associative-cued recall; SCR: Stem-cued recall; CRN: Context recognition; CCR: Context-cued recall; IRN: Item recognition; R: Remember; K- Know.

For the clinical control group, the main effect of the within-subject factor was significant, F (4, 45) = 5.32, p < .001, controls remembered fewer items in ACR verbal condition relative to CRN verbal and IRN visual conditions. The same, but smaller, main effect was found in the right frontal group, F (4, 45) = 2.00, p = .05, due to the poor performance in the ACR visual condition relative to CRN visual condition. For the left frontal group, the main effect task type factor was significant, F (4, 45) = 2.38, p < .05. This effect was due to the general poor retrieval rate in both ACR conditions relative to CRN conditions. The same repeated measure ANOVA was conducted for the right temporal group, revealing a significant main effect, F (4, 45) = 2.47, p < .05, due to the right temporal patients remembering fewer items in ACR visual condition than in SCR verbal condition. Finally, for the left temporal group, the repeated measure ANOVA revealed no significant differences, F (4, 45) = 1.89, p > .05.

3. 4. 4. Contrasting lateralization hypothesis

In order to separately examine the four lateralization hypotheses, we merged the respective tasks and performed separate mixed ANOVAs for each hypothesis. To test the separate effect of laterality (right vs. left) and localization (frontal vs. temporal), we examined the effect of these two factors separately in the following statistical analyses.

3. 4. 4. 1. Verbal-Visual Hypothesis

The merged dependent Verbal factor was formed from the mean scaled scores of ACR verbal, SCR verbal, IRN verbal, CRN verbal, and CCR visual tasks, whereas the dependent Visual factor was composed of ACR visual, SCR visual, IRN visual, CRN visual, and CCR visual scores. A 2 (Task type: Verbal vs. Visual) x 2 (Lateralization: Right vs. Left) x 2 (Localization: Frontal vs. Temporal) mixed ANOVA was conducted. The interaction of these three factors was not significant, F (1, 38) = 1.36, p > .05. The interaction of the task type and lateralization factors was also not significant, F (1, 38) = 3.07, p > 0.05, but the interaction effect of task type and localization factors was significant, F (1, 1) = 5.78, p < .05. There was no main effect of task type F (1, 38) = .01, p > .05, localization F (1, 38) = 2.34, p > .05, or lateralization F (1, 38) = 1.32, p > .05; however, the interaction between lateralization and localization was significant, F (1, 38) = 7.12, p < .05.

One-way ANOVA was conducted with groups as the independent factor, revealing significant differences only in Visual condition, F (1, 45) = 2.68, p = .05. The right frontal group retrieved significantly fewer items than did the control and left frontal groups (see Fig. 3.3).

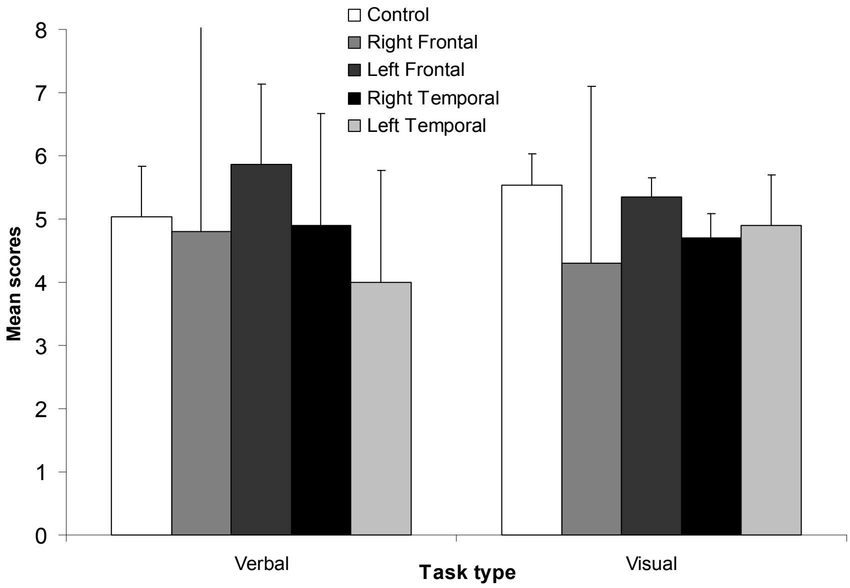


Figure 3. 3. Contrasting group performances on Verbal vs Visual factor. Error bars indicate standard deviation.

3. 2. 4. 2. HERA model

The merged dependent Encoding factor was formed from the mean scaled scores of ACR verbal and ACR visual tasks, whereas the dependent Retrieval factor was composed of SCR verbal, SCR visual, CRN verbal, CRN visual, CCR verbal, and CCR visual scores. A 2 (Task type: Encoding vs. Retrieval) x 2 (Lateralization: Right vs. Left) x 2 (Localization: Frontal vs. Temporal) mixed ANOVA was conducted. The interaction of these three factors was not significant, F (1, 38) = .97, p > .05. The interaction of task type and lateralization factors (F (1, 38) = .30, p > .05) and the interaction of task type and localization factors (F (1, 38) = .51, p > .05) were also not significant. The main effect of task type was significant (F (1, 38) = 14.11, p < .001), but the main effects of the localization (F (1, 38) = .49, p > .05) and lateralization (F (1, 38) = .57, p > .05) factors were not significant.

One-way ANOVA was conducted with groups as the independent factor, revealing significant differences only in Retrieval condition, F (4, 45) = 4.15, p = .01. The right frontal and left temporal groups retrieved significantly fewer items than did the control and left frontal groups (see Fig. 3.4).

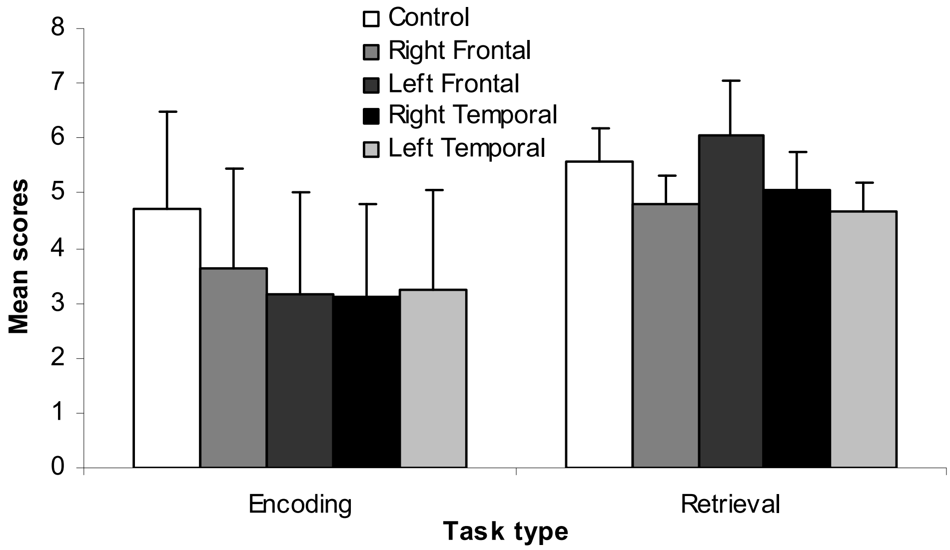


Figure 3. 4. Contrasting group performances on Encoding vs.Retrieval factor. Error bars indicate standard deviation.

3. 2. 4. 3. Systematic –Heuristic hypothesis

The merged Systematic factor was formed from the mean scaled scores of SCR verbal, SCR visual, CRN verbal, CRN visual, CCR, verbal and CCR visual tasks, whereas the Heuristic factor was composed of ACR verbal, ACR visual, IRN verbal, and IRN visual averaged scores.

A 2 (Task type: Systematic vs. Heuristic) x 2 (Lateralization: Right vs. Left) x 2 (Localization: Frontal vs. Temporal) mixed ANOVA was conducted. The interaction of these three factors was not significant, F (1, 38) = .73, p > .05. The interaction of task type and lateralization factors (F (1, 38) = .69, p > .05) and the interaction of task type and localization factors (F (1, 38) = .62, p > .05) were also not significant. There was a main effect of task type, F (1, 38) = 9.35, p < .05, but the main effects of localization (F (1, 38) = 2.05, p > .05) and lateralization (F (1, 38) = 1.35, p > .05) were not significant. Only the interaction between lateralization and localization showed significant differences, F (1, 38) = 4.68, p < .05.

One-way ANOVA was conducted with groups as the independent factor, revealing significant differences only in Systematic condition, F (4, 45) = 3.53, p < .05, due to the left frontal group retrieving significantly more items than did the left temporal group (see Fig. 3. 5).

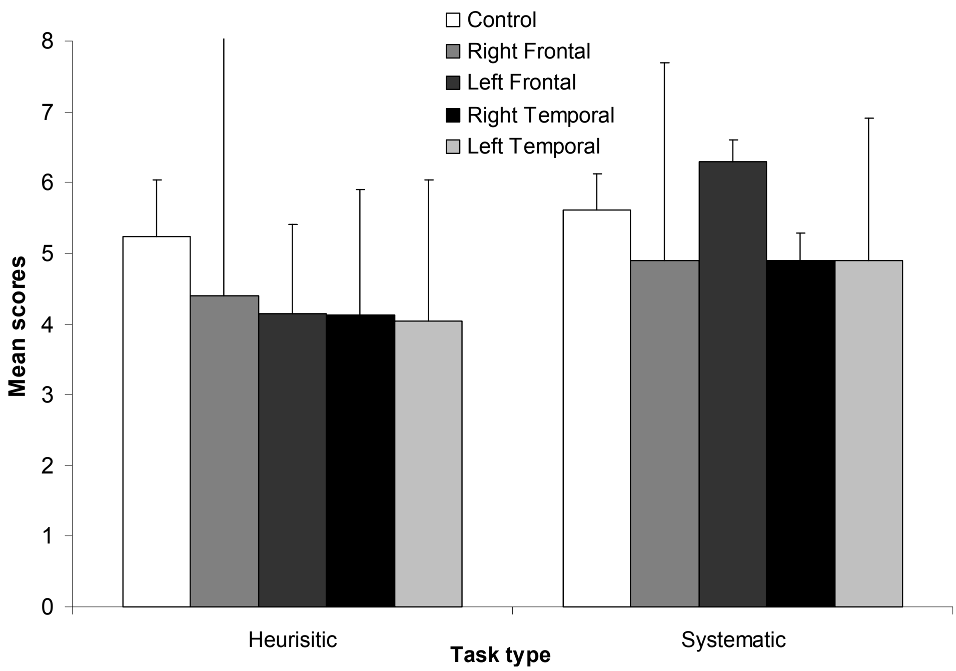


Figure 3. 5. Contrasting group performances on Systematic vs. Heuristic factor. Error bars indicate standard deviation.

3. 4. 4. 4. Production- Monitoring hypothesis

The merged dependent variables were the Production factor (ACR verbal, ACR visual, SCR verbal, SCR visual, CCR verbal, and CCR visual) and the Monitoring factor (IRN verbal, IRN visual, CRN verbal, and CRN visual).

A 2 (Task type: Production vs. Monitoring) x 2 (Lateralization: Right vs. Left) x 2 (Localization: Frontal vs. Temporal) mixed ANOVA was conducted. The interaction of these three factors was not significant, F (1, 38) = .43, $p > .05$. The interaction of task type and lateralization factors, F (1, 38) = 2.48, $p > .05$, and the interaction of task type and localization factors, F (1, 38) = 1.28, $p > .05$, were also not significant. There was a strong main effect of task type, F (1, 38) = 18.72, $p < .001$. However, the main effects of localization (F (1, 38) = 3.10, $p > .05$) and lateralization (F (1, 38) = 2.10, $p > .05$) were not significant, only the interaction of these two factors was significant, F (1, 38) = 8.31, $p < .05$.

One-way ANOVA was conducted with groups as the independent factor, revealing significant differences only in Recognition condition, F (4, 45) = 3.24, $p < .05$. The right frontal group retrieved significantly fewer items than did the left frontal group (see Fig . 3. 6).

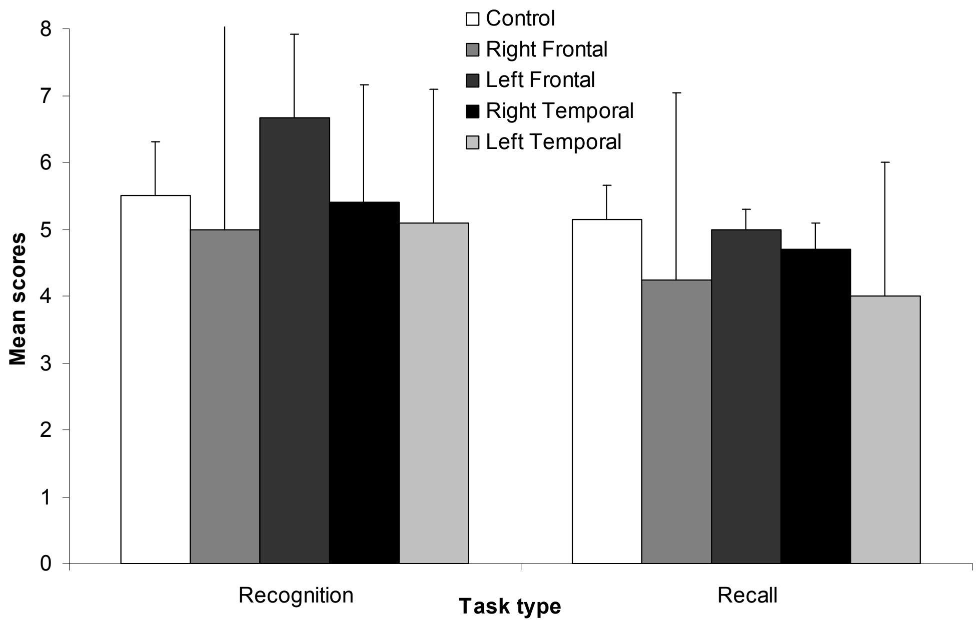


Figure 3. 6. Contrasting group performances on Production vs. Monitoring factor. Error bars indicate standard deviation.

3. 4. 5. Common components of the episodic memory tasks

In order to determine the possible common components of the episodic memory tasks, we performed a Principal Component Analysis (PCA; with an oblique Promaxrotation to allow for the possibility that these components might be correlated) on 14 dependent variables (the 10 episodic memory tasks plus the separated Remember/ Know responses in the two IRN tasks). A four-component solution was obtained; the four components accounted for 65% of the total variance (see Table 3. 3).

Component 1 included ACR verbal, ACR visual, SCR verbal, and SCR visual, corresponding to the ‘‘Production’’ factor of the hypothesis of Cabeza et al. (2003). Component 2, including the CCR verbal, CCR visual, IRN verbal/ Remember responses, and IRN visual/ Remember tasks, was the same as the "Monitoring" factor of the production- monitoring hypothesis, without the two CRN tasks (Cabeza et al., 2003). Component 3 included Know responses from the two IRN tasks; therefore, it may be considered a "Familiarity effect" factor. Finally, Component 4 was a clear "Contextual" component because it consisted of the four contextual tasks: CRN verbal, CRN visual, CCR verbal, and CCR visual.

Table 3. 3. Result of PCA on the 14 episodic memory tasks

	Principal components			
	Component 1	Component 2	Component 3	Component 4
ACR verbal	**.74**	-.53	.14	.06
ACR visual	**.68**	-.17	-.50	-.01
SCR verbal	**.59**	-.07	.50	-.24
SCR visual	**.62**	-.30	-.02	-.18
CRN verbal	-.33	-.15	-.09	**.34**
CRN visual	-.01	.09	.01	**.79**
CCR verbal	.20	.24	-.58	**.26**
CCR visual	.23	.40	-.37	**.64**
IRN verbal	.46	**.59**	.44	.33
IRN visual	.49	**.56**	.07	-.59
IRN verbal R	.54	**.60**	-.11	.07
IRN verbal K	-.24	.09	**.58**	-.01
IRN visual R	.13	**.44**	-.18	-.59
IRN visual K	-.07	.08	**.45**	.28
% Variance	27.93	15.05	12.80	10.25

Note: The values in the columns are coefficients of the principal components that are related to each of the experimental tasks. ACR: Associative-cued recall; SCR: Stem-cued recall; CRN: Context recognition; CCR: Context-cued recall; IRN: Item recognition.

To summarize the main results of these analyses, it seems that beside Monitoring and Production factors postulated by the model of Cabeza et al. (2003), Contextual memory and Familiarity effects may separately play an important role in memory retrieval. Since Monitoring, Production, and Contextual memory factors can be considered as executive function-related factors, in the second part of the statistical analysis, we concentrated on the relation between executive functions and episodic memory tasks.

3. 5. General Discussion

The findings that patients with left PFC injuries exhibited the highest performances on recognition tasks, whereas right PFC group performed better on the recall than on the recognition tasks support the production-monitoring hypothesis (Cabeza et al., 2003). The result of PCA analysis performed on experimental tasks provided evidence of four factors. Two of the factors, the Monitoring and Production factors, were similar to the two main factors postulated by the model of Cabeza et al. These results fit the idea that the right PFC is more involved in monitoring operations, including the evaluation and verification of recalled information, whereas the left PFC is more involved in semantically guided information production processes (Cabeza et al., 2003). The observed recall pattern in PFC groups is also consistent with the idea that the left hemisphere makes inferences and generalizations that go beyond available information, whereas the right hemisphere is less capable of inferences and generalizations, and is, hence, more veridical (Metcalfe, Funnell, & Gazzaniga, 1995; Nolde et al., 1998b; Cabeza et al., 2003). According to the production-monitoring hypothesis, this effect would be a clear example of what happens when semantically guided production processes mediated by the left PFC are not checked by monitoring and verification processes mediated by the right PFC. Whereas previous research with split brain did not determine whether these differences reflect the function of anterior or posterior brain regions, our present results suggest that they are related to the role of the left and the right PFC during the retrieval phase of episodic memory.

Besides sustaining the validity of the "production-monitoring" hypothesis, the results provide evidence for heuristic-systematic dissociation after temporal lobe injury. Patients with left temporal injury exhibited the poorest performance in SCR verbal and CRN verbal tasks in comparison with the other groups, whereas within–subject comparison revealed that the right temporal group displayed the poorest performance in the ACR visual condition (heuristic task) and performed relatively well in SCR conditions (systematic task). These results are in accord with the "heuristic-systematic" hypothesis postulated by Nolde et al. (1998b). Contrasting the lateralization hypothesis by separately analyzing the factors postulated by the different theories, a significant difference was found in the merged Systematic factor between the left frontal group, with the best performance, and the left temporal group, exhibiting the poorest performance. Previous functional neuroimaging studies of episodic retrieval have typically found differences in MTL activity as a function of type of episodic information recovered (Cabeza et al., 2001) and also of episodic retrieval task employed (Cabeza et al., 2003). Although the type of cognitive process that underlies the role of the hippocampus in episodic memory retrieval is unclear, one candidate process is the integration of perceptual aspects of retrieved information and retrieval cues. Perceptual integration can be considered as a systematic process because it requires binding together all information and, then, a systematic match/mismatch analysis. The process of perceptual integration is important for CRN and CCR because decisions in these tasks depend on the match/mismatch between the sensory properties of studied and test items. Perceptual integration is also important for the SCR situation because the words and images generated in the task must match the orthographic and visual structure of the word- or picture-stem cues. This systematic process seems to be more affected after left temporal lobe injury, while right temporal lobe injury influences the performance in more heuristic tasks, such as ACR or IRN. Although the systematic-heuristic dissociation seems to accommodate the present retrieval pattern in temporal groups, this idea is speculative and may not fit with other ideas regarding hippocampal function.

We found no clear evidence for Verbal/Visual dissociation. It seems as though this factor has only a moderating effect on retrieval. Regarding the HERA model, there is some evidence for the emphasized role of the right frontal lobe in retrieval. Comparison of the merged Encoding and Retrieval factors revealed that the right frontal group retrieved significantly fewer items than the left frontal groups, but we have found no evidence for the role of the left hemisphere in the encoding processes.

Although the present results are more consistent with the production-monitoring hypothesis than with the other hypotheses, these other hypotheses are not completely incompatible with our data. For example, the familiarity-based decisions that often occur in old–new recognition tasks are heuristically based (Nolde et al., 1998b; Johnson & Raye, 2000). All of the hypotheses, therefore, predict right PFC activity during such familiarity-based recognition judgments.

However, our present results suggest that the production-monitoring distinction provides a more complete and parsimonious account of the lateralization of PFC activity during episodic retrieval, whereas the systematic heuristic dissociation is more likely to explain the lateralization effect after temporal lobe injuries.

Results from PCA analysis provide evidence suggesting that besides monitoring and production processes, contextual memory and familiarity effect may have an important role in memory retrieval as separate factors. Furthermore, the lateralization of injuries significantly influenced the rate of “know” responses in IRN tasks, resulting in a higher rate of “know” responses after left hemisphere injuries. These results support Rugg’s dual-process model in light of the proposal that recollection is a continuous, rather than a discrete, memory process (Rugg & Curan, 2007; Vilberg & Rugg, 2007; Vilberg & Rugg, 2008a; 2008b). The results provide further evidence to support the idea that recollection- and familiarity-based recognition are dependent on distinct cortical networks: on the "parietal" and "mid-frontal" old/new effects, respectively (Yonelinas, 2002; Vilberg & Rugg, 2008a). In exploring the functional roles of the parietal and frontal regions, Vilberg and Rugg (2007, 2008a, 2008b) emphasize the role of the parietal regions (in addition to the frontal regions) in episodic memory retrieval. In an ERP study they have demonstrated that the "left-parietal old/new effect" is modulated by the amount of information retrieved, and proposed the explanation that retrieval-related activity in the left inferior parietal cortex reflects processes supporting the online representation of retrieved episodic information (Vilberg & Rugg, 2008b).

Future research will help to refine the lateralization hypotheses presented above so that they can capture more general aspects of the function of the left and right PFC and MTL, and eventually may be extended to other brain regions, such as the parietal cortex, as well as to other cognitive domains.

4. COMMON COMPONENTS OF THE EXECUTIVE FUNCTIONS

A question of central importance to the understanding of higher order cognition concerns the nature of the executive control and its neural implementation in the brain. Although much studied, the concept of the executive function or cognitive control remains elusive.

There is however an emerging consensus in the literature for the need to fractionate the early conception of the unitary 'central executive' (Baddeley & Hitch, 1974) and recent models have posited a view of executive functions as a conglomerate of largely independent, but constantly interacting control processes such as interference resolution, attention-shifting, updating, refreshing and inhibition (Solhlberg & Mateer, 1989; Johnson, 1992; Lezak, 1995; Baddeley, 1996; Fuster, 1997; Smith & Jonides, 1999; Callahan & Hinkebein, 1999; Miyake et al., 2000; Friedman & Miyake, 2004; Marklund et al., 2007). However, for models purporting to describe the executive functions, there is a striking lack of concordance. Table 4. 1 presents four models of executive functions for side-by-side comparision.

Table 4.1. Representative models of executive functions

Sohlberg & Mateer (1989)	**Lezak (1995)**	**Callahan (2000, 2001)**	**Miyake et al. (2000)**
Anticipation	Volition	Initiation	Shifting
Goal selection	Planning	Termination	Updating/monitoring
Planning	Purposive action	Self-regulation	Inhibition
Initiation of activity	Effective performance		
Self-regulation/ monitoring			
Use of feedback			

Overall, these „processing" approaches take the view that executive control can be described in terms of performance without specifying the representation that underlies these processes.

A common characteristic of these executive models is that the postulated executive subprocesses are considered (at least implicitly) to be domain general in the sense that they can come into play in a broad range of distinct cognitive domains (e.g., attention, working memory, long-term memory). By this view, the engagement of a particular executive function (e.g., inhibition) within any one cognitive task is simply a matter of the degree to which load is exercised on the operations ascribed to that control mechanism and should extend to any cognitive challenge that incorporates sufficient control requirements of the same kind.

In our studies we used the executive components model of Miyake et al. (2000), because it provides the necessary empirical basis for developing a theory that specifies how executive functions are organized and what roles they play in complex cognition. In Miyake and his collegues' model three executive functions were defined with metaanalysis as basic components: (a) shifting between tasks or mental sets, (b) updating and monitoring of working memory representations, and (c) inhibition of dominant or prepotent responses. These three functions are frequently postulated in the literature as important executive components (e.g., Baddeley, 1996; Smith & Jonides, 1999, Miyake, 2000). All three are relatively circumscribed, lower level functions (in comparison to some other often postulated executive functions like ''planning'') and hence can be operationally defined in a fairly precise manner. Furthermore, these three target functions are likely to be implicated in the performance of more complex executive tests, like the Wisconsin Card Sorting Test (WCST), Tower of London (TOL), Random Number Generation (RNG) and other tests (see Miyake et al., 2000), altough each target function can be taped separately with a number of well studied, relatively simple cognitive tasks.

There are obvious dangers in postulating an unlimited number of executive processes. Simply inventing new tasks on a priori principle and then nominating them as measures of basic executive processes is clearly not a satisfactory solution to the problem of analysing the executive functions. In due course, when adequate measures of a number of supposedly different executive processes have been developed, it is necessary to carry out larger scale correlational studies using patients who are likely to have a range of executive problems. If we have been succesful in isolating a number of separable executive processes, then we would expect a higher correlation across different tasks that are assumed to measure the same process with a clear separation from other clusters of the proposed executive processes.

Thus, the main purpose of the studies from this section was to examine the relation between the different executive components and episodic memory functions, using newly developed executive-memory tests (Section 4.1), classic neuropsychological tests, and previously presented, experimental paradigms measuring automatic/ intentional inhibition, and production/ monitoring processes during episodic memory retrieval (Section 4.2 and Section 4. 3)

4.1. The executive indices of The 7 Courses Memory Test

The 7 Courses Memory Test was developed initialy by A. Verseghi in 1992, and then revised, standardized and published by A. Verseghi and M. Albu (2004, 2005, 2006).

This test has been designed to examine visual-spatial memory, executive functions and their interactions in people with acquired brain injury. The test provides a scoring method for the temporal organization of memory items, effect of stimuli frequency, proactive and retroactive interference.

The present study aims to define beside the standard memory indices some useful indices for measuring executive functions by using simultaneously qualitative and quantitative analyis.

4. 1. 1. Method

4. 1. 1. 1. Participants

Various groups of normal controls (N = 88) and brain injured patients (N =116), both men and women, aged between 17 to 60, with different lateralization and localization (left- and right frontal, left- and right posterior, left- and right temporal) were examined. The patients were recruited from the National Institute for Medical Rehabilitation, Head- and Brain Injury Department in Budapest, Hungary. Subjects older than 60 years, with a native tongue other than Hungarian, time since onset smaller than 1.5 months or with history of psychiatric and/or other neurological disease were excluded. Patiens were selected upon a review of their medical records including computer tomography (CT) or magnetic resonance imagery (MRI). Specific details of lesions sites were not available and the medical notes indicated only laterality of injury and general extension, so we used only the lateralization of injury (left or right) as independent variable.

4. 1. 1. 2. The 7 Courses Memory Test

The test includes recognition tasks (Courses 1-6) becoming gradually more and more difficult, and an incidental spatial recall task (C. 7). In series 1 - 4 the task is to retain and recognize four different goal stimuli in all four series from among 17 pictures presented sequentially. In "courses" 5 and 6 the person is simultaneously presented 17 pictures in a 4 x 4 + 1 spatial arrangement from which s/he has to recognize those pictures that have never been selected and recognized in the first four series as goal stimuli (C. 5), and those that have been selected more than once before (C. 6). The first six "courses" provide a scoring method for the temporal organization of memory items, effect of stimuli frequency, memory inhibition and self monitoring.

Beside right answers, false alarms and omissions, we have calculated the subjective percentage of false alarms (FA*) and omissions (O*), according to persons` previous answers. This is done according to the following formula: [FA*[1]/ (H*[2] + FA*)]. In same way we calculated 5* and 6* Omissions, the subjective percentage of omissions according to persons` previous answers with the following formula [O*[3]/ (H* + O*)].

Beside quantitative measurements, specific error types were defined by qualitative analysis (see table 4.2).

Table 4. 2. Specific error types in The 7 Courses Memory Test

Error types	Definition
Perseverations 1 (P1)	Re-choosing a correctly chosen item in later series
Perseveration 2 (P2)	Re-choosing a falsely chosen item in later series
Perseveration 3 (P3)	Choosing a second (or more) item following a chosen one within the series
Delayed Activisation (DA)	Choosing the omitted item in the next series or choosing the item consecutive of the missed target item
4 and 5 Together	Choosing the same item in Series 4. and 5
5 and 6 Together	Choosing the same item in Series 5. and 6
Disparition of Multiple Significance in C.5. (DS)	Choosing an item in Series 5 which has already been chosen by the person several times as goal stimulus in S.1 - 4
Overestimation of a Neutral Stimulus in C.6 (OS)	Choosing an item in Series 6. which has never been chosen before by the person as goal stimulus in S.1 - 4
Lost Structure in C.7 (LS)	Loosing the 4 x 4 + 1 structure in the spatial task

[1] False Alarms according to person`s previous answers
[2] Hits according to person`s previous answers
[3] Omissions according to persons` previous answers

4. 1. 2. Results and Discussion

Table 4. 3. gives means and standard deviation for each of the 7 steps measures (Right Answers, False Alarms, Omissions) and for different specific error types.

Table 4. 3. Performance and specific errors of all subjects in the 7 "courses"

	Control subjects (N=88)	Subjects with left hemisphere injury (N=68)	Subjects with right hemisphere injury (N=48)
1-4 Hits	14.9 (1.2)	12.39 (2.74)	11.52 (3.00)
1-4 False Alarms	1.01 (1.26)	4.56 (4.06)	6.00 (5.29)
5. Hits	2.56 (.63)	2.03 (.87)	1.88 (.98)
5. False Alarms	1.13 (1.21)	3.00 (2.07)	2.87 (2.15)
6. Hits	1.44 (.64)	1.19 (2.65)	.76 (.65)
6. FalseAlarms	1.2 (1.3)	2.59 (2.39)	2.98 (2.13)
7. Spatial Task	12.56 (3.22)	8.83 (3.74)	6.44 (4.2)
5. Subjective False Alarms	.17 (.22)	.36 (.23)	.40 (.32)
5. Subjective Omission	.21 (.21)	.26 (.24)	.39 (.32)
6. Subjective False Alarms	.31 (.33)	.36 (.27)	.48 (.35)
6. Subjective Omission	.32 (.33)	.38 (.31)	.55 (.33)
Perseveration 1	.28 (.32)	1.53 (1.82)	1.51 (1.37)
Perseveration 2	.04 (<.01)	.45 (.95)	.51 (.88)
Perseveration 3	.06 (<.01)	.84 (1.39)	1.23 (1.77)
Delayed Activisation	.03 (<.01)	.56 (.89)	.79 (1.16)
4 and 5 Together	.07 (<.01)	.32 (.77)	.44 (.88)
5 and 6 Together	.01 (<.01)	.07 (.34)	.31 (.75)
Disparation of Significance	.04 (<.01)	.30 (.61)	.49 (.90)
Overestimation of N. Stimuli	.04 (<.01)	.26 (.87)	.23 (.47)
Lost Stucture	.01 (<.01)	.08 (.24)	.41 (.50)

As a result of both qualitative and quantitative analysis, the control and brain injured persons are well differentiated by each "courses" of the task and specific error types proved to be characteristic of brain injured patients (all t's (203) > 4.00 and all p's < .001). Furthermore, groups with different lateralization can be separated based on the true answers and false alarms in Steps 1 - 6 and in spatial Step 7 which is especially sensible to damages of the right hemisphere. We found significant differences between left- and right side injured patients in C.5. Subjective Omissions, $t (105) = 2.51$, $p< .01$; C.6. Hits, $t (105) = 3.25$, $p< .01$; C.6. Subjective Omissions, $t (105) = 2.77$, $p< .01$, and in C.7, $t (105) = 3.19$, $p< .01$.

A between group comparision revealed also that various error types are more common in brain injured persons with right lateralization than with left lateralization, but the differences between the two patient groups were significant only in 5 and 6 Together, $t (105) = 3.25$, $p= .02$, and in Lost Structure errors, $t (105) = 4.83$, $p< .01$, respectively.

Specific error types were analyzed as possible indices of executive functions by performing Principal Component Analysis (PCA; with an oblique Promaxrotation to allow for the possibility that these components might be correlated) on 13 dependendent variables. We obtained two separate components: an Inhibition Component including Perseveration 1 (P1), Perseveration 2 (P2), Perseveration 3 (P3) and Delayed Activisation (DA), and a Self-monitoring Component including Delayed Activisation, Disparition of Significance (DS), and C.5. Subjective False Alarms (C.5. FA*), C. 5. Subjective Omissions (C.5. O*) and C. 6. Subjective Omissions (C.6. O*).

From these variables we computed two separate indices: the Inhibition Index (I-I) and the Self-Monitoring Index (SM-I). The Inhibition Index was calculated according to the following formula: I - I = (Max Hits -P1 - P2 - P3 – DA) / Max Hits. In same way we calculated the Self-Monitoring Index: SM – I = (Max Hits – DA – DS – C.5.FA* - C.5.O* - C.6. O*) / Max Hits. Mean values of these two executive indices vary between -1 and 1 with a score of 0 or bellow indicating disrupted executive functioning and a score of 1 total inhibition or self-monitoring (see Figure 4.1).

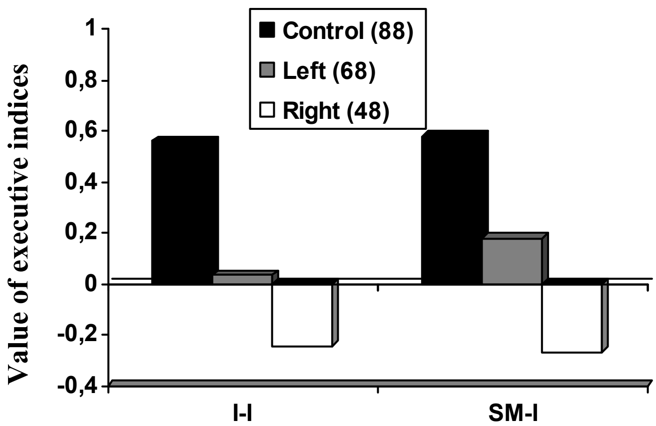


Figure 4. 1. Inhibition- and Self-Monitoring indices. Mean values of these two executive indices vary between -1 and 1 with a score of 0 or bellow indicating disrupted executive functioning and a score of 1 total inhibition or self-monitoring.

We have compared the performances of control and brain-injured persons, and we found significant differences in both of the executive indices: $t(203) = 5.4$, $p < .001$ and $t(203) > 4.6$, $p < .001$, respectively The right hemisphere injured patients are clearly more impaired and showed no inhibition and self-monitoring in comparision with the left hemisphere injured patients, but the difference between these two groups was significant only in Self – Monitoring ability, $t(105) = 2.18$, $p < .05$.

In summary, the data show that as a result of both qualitative and quantitative analysis, the healthy and brain injured persons are well differentiated by each measures of the test. Furthermore, groups with different lateralization can be separated on the basis of their quantitative scores (hits and false alarms in the 7 "courses") and specific error types: the patients with right hemispehere injury showing more impaired performance in comparison to patients with left hemisphere injury. Additionally, since specific error types indicated a dysfunction in the executive system, using PCA we defined two executive indices: Inhibition and Self-monitoring. The comparison of these two indices indicated that the right hemisphere injured patients are clearly more impaired and showed no inhibition and self-monitoring in comparison to the left hemisphere injured patients.

Thus, The 7 Courses Memory Test has proved to be adequate at a quick screening as well as at a detailed analysis of memory- and executive components.

4. 2. Inhibitional component of the executive functions

In classical neuropsychological cases, a deficit of inhibition was described in frontal lobe patients since the famous case of Phineas Gage (Harlow, 1868; Milner, 1964; Damasio, 1996; see Stuss, 1991, for review). Lurija (1966, 1973) also decribed particular signs of disinhibition (perseverations, stereotypes, behavioural disinhibition, etc.) in patients with large frontal lobe lesions. The inhibition component of the executive functions appears in almost all of the executive models. For example the inhibition was considered by Norman and Shallice (1980) as one of the main SAS or executive functions; similarly, Baddeley (1996) emphasised inhibition as one of the two main functions of the central executive and it was defined by metaanalysis as one of the basic executive functions (Miyake et al., 2000). Overall, neuropsychological researchers have suggested that the deficit of the inhibitory mechanisms is specifically associated with frontal lobe lesions, especially with right sided lesions (e.g. Dempster, 1991; Shallice, 1988;

Shimamura, 1995, 2000; Conway & Fthenaki, 2003; Albu, Racsmany, Conway, in press).

In this section evidence will be presented for the relationship between inhibition and right frontal cortex from neuropsychological test results and from inhibitory paradigms developed in Section 2.

4. 2. 1. Method

4. 2. 1. 1. Participants

The same brain injured and control groups (13 subjects with right frontal lobe lesion, 11 subjects with left frontal lobe lesion, 12 subjects with unilateral temporal lobe lesion and 13 control subjects) participated in this study as in Section 2.1.-2. 4.

4. 2. 1. 2. Neuropsychological tests

In order to better characterize the patients with frontal- and temporal lobe lesions each subject was evaluated with several neuropsychological tests measuring working memory, episodic memory and executive functions.Working memory functions were evaluated with the Digit Span, and Digit-Backward Span subtest (Lezak 1995; Racsmány, Albu, Lukács, & Pléh, Cs. 2007), the Corsi Block Taping task (Lezak, 1995; Racsmány, Albu, Lukács, & Pléh, Cs. 2007) and the Working memory subtask from the Test of Attentional performance (TAP; Zimmermann & Fimm, 1993). This latter working memory task is a standard n-back pradigm (2-back condition). Episodic memory functions were assessed with the Rivermead Behavioral Memory Test (RBMT), designed to assess memory skills related to everyday situations (Wilson et al, 1985). 11 subtests measure many of the everyday memory problems reported and observed in patients. We used for statistical analysis the overall profile score of Version A. The executive functions were evaluated with the Behavioural Assesment of Dysexecutive Syndrome (BADS), a complex executive battery (Wilson et al, 1996). The BADS battery (Wilson et al, 1996) with six subtests was designed to assess the effects of dysexecutive syndrome, a cluster of impairments generally associated with damage to the frontal lobes of the brain. These impairments include difficulties with high-level tasks such as planning, organising, initiating, monitoring, time evaluating, rule-keeping, problemsolving and adapting behaviour. The six subtasks are: 1. Rule Shift Cards, testing the ability to change an established pattern of responding; 2. Action Program subtask testing practical problem solving; 3. Key search testing for strategy formation; 4. Temporal Judgment, assessing subjects ability to estimate how long various events last; 5. Zoo

Map is a test of planning; 6. Modified Six Elements is a test of planning, task scheduling and performance monitoring.General intellectual function was measured with the Raven Progressive Matrices (Raven, 1938).

4. 2. 1. 3. Inhibitory paradigms

We used the same four inhibitory paradigms as in Section 2.1.-2.4., namely the Stroop-task, the go/ no-go task, Directed Forgetting (DF) and Retrieval Induced Forgetting (RIF).

4. 2. 2. Results and Discussion

4. 2. 2. 1. Neuropsychological test results

Table 4.4 shows performances on neuropsychological tests. The number of participants included in each analysis is also presented. Seven of our brain-injured participants were unable to complete the entire neuropsychological battery because of time and technical constraints. However, every patient received a complete neuropsychological diagnosis based on measurements of his/her memory, executive functioning and intellectual abilities.

A one-way ANOVA and a post-hoc Sheffe – test revealed an interesting pattern in working memory tests: in the digit span and Corsi block tapping tasks the right frontal and temporal groups have had the most impaired performances, $F (3, 37) = 4.06$, $p = .01$ and $F (3, 39) = 3.51$, $p< .01$; while the digit –back task was especially sensitive to the frontal lobe lesions, $F (3, 38) = 6.89$, $p = .01$. In the n-back paradigm the right frontal group showed the most impaired performance and the left frontal group had the highest performance among the patient groups, $F (3, 37) = 4.74$, $p < .01$. In the Behavioral Assesment of the Dysexecutive Syndrome (BADS) the right frontal group was reliably poorer than the clinical control group, $F (3, 33) = 3.05$, $p < .05$. The separate ANOVA and post-hoc Sheffe analysis of the subtasks revealed that the right frontal group was reliably poorer in Rule Shifting, $F (3, 33) = 7.47$, $p < .01$; in Problemsolving, $F (3, 33) = 6.77$, $p < .01$ and in Keysearch subtasks, $F (3, 33) = 3.06$, $p < .05$. There were no significant differences between the groups in Raven Progressive Matrices Test, $F (3, 41) = 1.50$, $p > .05$.

Using two-way ANOVA-s on patients population with localization (frontal/ temporal lesions) and lateralization (right/ left lesions) as independent factors we found a significant interaction effect only in the 2-back paradigm, $F (1, 34) = 2.74$, $p < .05$; and the effect of localization was also significant, $F (1, 34) = 1.96$, $p < .05$.

Table 4. 4. Demographical and neuropsychological characteristics of the groups

	Right Frontal lesion group	Left Frontal lesion group	Unilateral temporal lesion group	Control group
Digit Span	6.00 (1.18) N=11	6.88 (1.53) N=9	6.11 (.6) N=10	7.26 (.22) N =13
Corsi Block Tapping Span	4.45 (.93) N=11	4.66 (.70) N=9	4.3 (.94) N=10	5.56 (.62) N =13
Digit- backward Span	4.18 (1.16) N=11	4.75 (1.03) N=9	5.6 (1.71) N=10	5.92 (1.16) N =13
2-back (max.15)	8.87 (3.35) N=8	13.87 (4.48) N=9	10.83 (3.61) N=12	13.58 (1.37) N =13
RBMT (max. 24)	16.91 (4.20) N=11	15.5 (5.18) N=8	16.8 (5.90) N=10	23.69 (.63) N =13
BADS (max.24)	13.30 (3.09) N = 10	15.17 (2.40) N = 6	15.22 (4.49) N = 9	17.50 (2.60) N = 12
BADS 1- Rule Shift (max.4)	2.10 (1.59) N = 10	3 (1.09) N = 6	3.56 (0.52) N = 9	4.00 (0) N = 12
BADS 2 – Problemsolving (max.4)	2.9 (.74) N = 10	3.83 (.40) N = 6	3.67 (0.52) N = 9	3.83 (.39) N = 12
BADS 3 – Keysearch (max.4)	1.60 (.96) N = 10	2.33 (1.21) N = 6	2.67 (1.12) N = 9	2.83 (.83) N = 12
BADS 4 – Time Evaluation (max.4)	2.10 (.87) N = 10	1.13 (1.03) N = 6	1.89 (0.78) N = 9	1.67 (.98) N = 12
BADS 5 – Zoo-map (max.4)	2.40 (1.17) N = 10	2.17 (.75) N = 6	1.89 (.93) N = 9	2.33 (.65) N = 12
BADS 6 – Modified 6 Elements (max.4)	2.10 (1.10) N = 10	2.67 (.52) N = 6	2.00 (1.22) N = 9	2.83 (1.03) N = 12
Raven Standard Progressive Matrices (max. 60)	13.30 (3.00) N=13	15.17 (2.4) N=10	15. 67 (2.6) N=11	17.50 (2.61) N =13

Note: Table values are mean (S.D.). RBMT: Rivermead Behavioral Memory Test, BADS: Behavioral Assesment of the Dysexecutive Syndrome.

In the next step of the statistical analysis we focused on three executive functions of the executive model of Miyake et al. (2000): Shifting, Updating and Inhibition. Simple tasks were selected to tap each of these executive functions: for testing Shifting function we used the profile score from the BADS – Rule Shifting subtask; the number of hits from the 2-back working memory task span was used as the indicator of the Updating factor; and finally the Inhibition factor was measured with the number of errors in a paper-pencil version of the Stroop interference task. From these variables we computed three separate executive indices: the Shifting Index, the Inhibition Index and the Updating Index.

The Shifting Index was calculated according to the following formula: Shifting Index = (Max Hits – Errors)/ Max Hits. The Inhibition Index was calculated with the same formula: Inhibition Index = (Max Hits - Errors) / Max Hits. In same way we calculated the Updating Index: Updating Index = (Max Hits – Omissions) / Max Hits. Mean values of these two executive indices vary between 1 and 0 with a score of 0 indicating disrupted executive functioning and a score of 1 effective executive functions. We have compared the performances of control and brain-injured groups, and we found significant differences in Shifting and Inhibition indices: Shifting $F(3, 36) = 7.47$, $p < .001$ and $F(3, 36) = 4.07$, $p < .01$, respectively (see Figure 4.2). Differences in Updating function showed only a tendency toward significance, $F(3, 36)$ 2.27, $p < .1$. Post hoc Sheffe tests revealed that the right frontal group was clearly more impaired and showed no inhibition and shifting in comparision with the other groups.

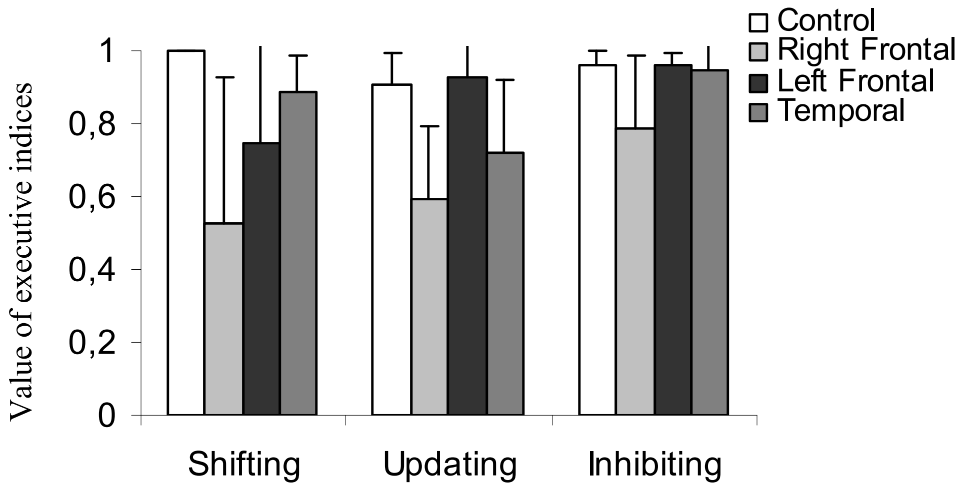


Figure 4. 2. Shifting-, Updating and Inhibition- indices. Mean values of these executive indices vary between -1 and 0 with a score of 0 indicating disrupted executive functioning and a score of 1 efficient executive functions. Error bars indicate standard deviations.

4. 2. 2. 2. Correlational analyses: Inhibition indices and executive components

The next step of the statistical analysis aimed to examine the relation between the inhibition indices and different executive functions measured with neuropsychological tests (see Table 4.5). First of all a correlational analysis was computed to assess for interrelationships between the following inhibition indices: DF cost index (Remember List 1 - Forgetting List1), DF benefit index (Forgetting List 2 - Remember List.2), RIF inhibition index (NRP items - Rp- items), Stroop RT interference index (RT in interference condition - RT in color naming condition), Stroop Errors interference index (Errors in interference condition - Errors in color naming condition); go/ no-go RT, go/ no-go desinhibition index (False Alarms). The DF cost index correlated negatively with the go / no-go RT ($r = -.31$; $p < .05$) and the RIF inhibition index correlated negatively with the Stroop RT interference index ($r = -.35$; $p < .05$). The go/ no - go desinhibition index showed a strong negative correlation with the go/ no-go RT ($r = -.52$; $p < .01$) and with Stroop RT interference index ($r = -.32$; $< .05$). No other correlations reached significance (r's < .3).

We were also interested in the relationships between each of these seven measures and the neuropsychological tests presented in Table 4. 5, measuring working memory, episodic memory and executive functions. The correlational results indicate that the Stroop Errors interference index correlated negatively with the 2-back task ($r = -.52$; $p < .05$). The go/ no-go RT showed negative correlations with the BADS overall score ($r = -.38$; $p < .05$), BADS - 1. Rule Shifting subtasks ($r = -.49$; $p < .01$) and BADS - 3. Key search subtask ($r = -.34$, $p < .05$), while the go/ no-go desinhibition index correlated positively with the RBMT profile score ($r = .40$; $p < .05$) and BADS - 3. Key search subtask ($r = .43$; $p < .05$). None of the neuropsychological measures correlated significantly with the DF cost effect (r's < .3), but DF benefit index exhibited significant correlation with BADS- Keysearch Subtask ($r = .32$; $p < .05$). The RIF inhibition index showed a positive correlation with the RMBT profile score ($r = .40$; $p < .05$) and a negative correlation with the BADS - 4. Time evaluation subtask ($r = -.33$; $p < .05$).

To examine these relations further, in the next step of the statistical analysis we performed correlational analysis between executive components and inhibition indices. Specifically, we focused on three executive functions of the executive model of Miyake et al. (2000): shifting, updating and inhibition. Simple tasks were selected to tap each of these executive functions: for testing Shifting function we used the profile score from the BADS – Rule Shifting subtask; the number of hits from the 2-back working memory task span was used as the indicator of the Updating factor; and finally the Inhibition factor was measured with the number of errors in a paper-pencil version of the Stroop interference task.

Table 4. 5. Correlation between the inhibition indices, executive indices and neuropsychological tests measuring executive functions

Inhibition indices	Stroop RT Interf.I	Stroop Errors Interf.I	Go/no-go RT	Go/ no-go FA	DF cost	DF benefit	RIF inhib. I.
Stroop RT Interf.I		.04	.20	**-.32**	.28	-.25	**-.35**
Stroop Errors Interf.I	.04		.04	-.09	-.21	.09	-.20
Go/no-go RT	.20	.04		**-.52**	**-.31**	-.21	-.01
Go/ no-go FA	**-.32**	-.09	**-.52**		.14	.18	.05
DF cost	.28	-.21	**-.31**	.14		.28	0
DF benefit	-.25	.09	-.21	.18	.28		.22
RIF inhib. I.	**-.35**	-.20	-.01	.05	0	.22	
Neuropsychological tests and executive indices							
Digit Span	.03	.17	-.14	.19	.10	.11	.13
Corsi Blocks Span	-.09	-.02	-.19	-.21	.10	.17	.08
Digit- backward Span	.27	-.03	-.22	.17	-.06	-.04	-.23
2-back /***Updating***	.22	**-.52**	-.12	.13	.10	.09	.12
RBMT	-.26	-.07	.26	**.40**	.17	.07	**.40**
BADS	.11	-.05	**-.38**	.13	-.10	.10	-.07
BADS 1- Rule Shift ***Shifting***	.09	-.32	**-.49**	.26	-.13	.07	.01
BADS 2 – Problemsolving	.13	-.06	-.26	0	-.05	.05	-.08
BADS 3 – Keysearch	.14	-.04	**-.34**	**.43**	-.04	**.32**	-.12
BADS 4 – Time Evaluation	.20	-.29	.15	-.36	-.22	-.17	**-.33**
BADS 5 – Zoo-map	.08	-.25	-.05	.05	0	.21	.29
BADS 6 – Modified 6 Elements	.04	.25	-.19	-.08	.12	-.19	-.04
Stroop task/ ***Inhibition***	.04	**.87**	.04	-.09	**-.32**	.09	-.20

Note: Significant correlation (p < .05) are highligted. I: Index; DF: Directed Forgetting; Interf.: Interference; RBMT: Rivermead Behavioral Memory Test, BADS: Behavioral Assesment of the Dysexecutive Syndrome.

Correlational studies were performed between inhibition indices and executive components indicator aiming to examine the supposedly different executive load of inhibition indices (see Table 4.5). The Shifting factor showed significant correlation only with the go/ no- go RT variable ($r = -.49$; $p < .05$). The Updating factor exhibited significant correlations with the desinhibition index of the Stroop- task ($r = -.52$; $p < .01$). Finally, the Inhibition factor was correlated with two indices: the DF cost index ($r = - .32$; $p < .05$) and the interference index of the Sroop task ($r = .87$; $p < .001$).

Summarizing the results, it can be emphasized that tasks measuring the CE component (like digit –back) were especially sensitive to the frontal lobe lesions, especially to the right sided lesion: for example in the n-back paradigm the right frontal group showed the most impaired performance. Correlation analysis revealed possible relations between some of the inhibition indices and executive functions measured with neuropsychological tests. As regards these correlations, it should be emphasised that from the inhibition indices the DF cost, go/ no- go RT and Stroop desinhibition indices exhibited a significant relationship with the measures of the different executive functions, while the RIF inhibition index and the Stroop task RT variable and the go/ no- go desinhibition index were related rather with episodic memory and working memory measures, probably being less loaded in executive functions than the other indices of inhibition.

4. 3. Lateralization of different executive functions

In the previous section we have seen that the inhibition component is related to the right frontal lobe functioning. Since the new executive models consider executive functions as a conglomerate of independent, but interacting control processes such as interference resolution, attention-shifting, updating, refreshing and inhibition, beside the inhibition in this section we shall examine another components of the executive system. In this context we used the production/ monitoring dissociation of memory retrieval processes, presented in Section 3, trying to found specific link between the examined executive processes and anatomical localization of this processes. The “production- monitoring” hypothesis proposes that the left PFC is primary involved in semantically guided production of information, while the right PFC is more active during monitoring processes.

Thus, the main purpose of the present correlational study was to examine the relation between the different executive components and episodic memory functions, using classical neuropsychological tests, and experimentally developed tasks measuring inhibition, updating, shifting components and also systematic/ heuristic and production/ monitoring processes.

4. 3. 1. Method

4. 3. 1. 1. Participants

The same 50 subjects (10 with right frontal lobe lesion, 10 subjects with left frontal lobe lesion, 10 subjects with right temporal lobe lesion, 10 subjects with left temporal lobe lesion and 10 clinical control subjects) participated in this study as in Section 3.

4. 3. 1. 2. Neuropsychological tests

Each subject was evaluated with several neuropsychological tests measuring working memory functions, episodic memory, executive functions and general intellectual functions.

Working memory functions were evaluated with the Digit Span, Digit-Backward Span (Lezak, 1995) and Corsi Block Taping tasks (Lezak, 1995). For measuring episodic memory functions Doors and People Test was used with four different subtasks (Baddeley, Emslie & Nimmo-Smith, 1994), yielding separate measures for visual and verbal memory, recall and recognition, and forgetting. Executive functions were evaluated with Stroop task (Stroop, 1935) and with Behavioral Assessment of Dysexecutive Syndrome (BADS), a complex executive battery (Wilson et al, 1996). A computerized version of Stroop task was used, with three conditions: color-naming, reading and incongruent color naming, measuring the reaction times and the committed errors. The BADS battery (Wilson et al, 1996) with six subtests was designed to assess the effects of dysexecutive syndrome, a cluster of impairments generally associated with damage to the frontal lobes of the brain. These impairments include difficulties with high-level tasks such as planning, organising, initiating, monitoring, time evaluating, rule-keeping, problem-solving and adapting behaviour. General intellectual function was measured with the Raven Progressive Matrices (Raven, 1938).

4. 3. 1. 3. Experimentally developed executive tasks

1. Plus–minus task was used for measuring the shifting component of Miyake and his collegues' (2000) model. The plus–minus task, adapted from Jersild (1927), Spector and Biederman (1976) and Miyake et al. (2000) consisted of three lists of 30 two-digit numbers (the numbers 10–99 prerandomized without replacement) on a single sheet of paper. On the first list, the participants were instructed to add 7 to each number and write down their answers. On the second list, they were instructed to subtract 7 from each number. Finally, on the third list, the participants were required to alternate between adding 7 to and subtracting 7 from the numbers (i.e., add 7 to the first number, subtract 7 from the second number, and so on). For each list the subjects had 1 minute to complete, and the number of performed arithmetic operations was used for calculating the shifting cost. The cost of shifting between the operations of addition and subtraction was calculated as the difference between the number of completed operations from the alternating list and the average of the number of completed additions and substractions. This shift cost served as the dependent measure.

2. The maximum number of correctly recalled spans in **Digit- Backward task** was used as the indicator of refreshing component of the executive model of Miyake et al. (2000).

3. A computerized version of the **Stroop task** was aborted for evaluating the inhibition component of executive components model (Miyake et al, 2000). The color naming condition of the Stroop task consisted in 60 XXXXX items colored red, blue, green or yellow. The reading condition consisted of 60 color-name words (RED, BLUE, GREEN, YELLOW) written in black ink, and the interference condition was the standard Stroop incongruent color naming condition: the words RED, BLUE, GREEN, YELLOW were written 60 times in a color different from the meaning of the word. The difference in reaction times between interference and color naming condition and the errors in interference condition were taken as dependent variables.

4. 3. 1. 4. Episodic memory tasks

The same ten episodic retrieval tasks were used as in Section 3: verbal and visual associative cued recall (ACR), verbal and visual stem-cued recall (SCR), verbal and visual item recognition (IRN), verbal and visual context recognition (CRN) and recall (CCR), testing differentialy for systematic/heuristic and production/ monitoring processes (see also Figure 3.2)

4. 3. 2. Results and Discussion

4. 3. 2. 1. Neuropsychological tests results

Table 4.6 shows the characteristics of patient- and clinical control groups, and their performance on neuropsychological tests.

One- way ANOVAs on the four patient- and the clinical control groups yielded significant difference between groups in several neuropsychological tests. It can be seen from Table 4. 6 that the frontal lobe patients scored within the normal range on working memory tests, but exhibited impairments on the neuropsychological tests that have been shown to be sensitive to frontal lobe injury, especially to patients with right frontal lobe injury. All groups of patients showed impaired performances in the long-term episodic memory test.

Table 4. 6. Performance on neuropsychological tests and in executive tasks of all subjects

	Right Frontal lesion group (N = 10)	Left Frontal Lesion group (N = 10)	Right Temporal lesion group (N = 10)	Left Temporal lesion group (N = 10)	Clinical control group (N = 10)
Digit Span	6.16 (1.17)	6.16 (1.17)	5.80 (1.75)	6.16 (.69)	6.00 (.75)
Digit-Backward	4.33 (1.03)	4.83 (.40)	4.80 (.81)	4.66 (1.27)	4.62 (.9)
Span -***Updating***					
Corsi Blocks Span	4.66 (.51)	4.83 (.75)	5.00 (.98)	5.00 (.95)	5.12 (.64)
Doors & People (max.120)	63 (17.52)	62 (23.92)	64.77 (24.11)	55.75 (17.5)	94.8 (16.66)
BADS (max.24)	12.88 (3.21)	16.4 (3.37)	14.87 (3.84)	15.2 (3.96)	19.62 (3.66)
Stroop (Error)	7.60 (7.50)	.66 (1.00)	2.50 (2.62)	3.09 (3.02)	1.42 (2.51)
Inhibition					
Plus/minus task	1.4 (2.07)	2.12 (3.01)	3.00 (3.20)	1.50 (2.55)	3.43 (3.22)
Shifting					
Raven SPM	51.66 (1.15)	47.00 (5.62)	50.00 (5.13)	43.87 (7.56)	51.87 (5.91)

Note: Table values are mean (S.D.) BADS: Behavioral Assesment of the Dysexecutive Syndrome, Raven SPM: Raven Standard Progressive Matrices

One-way ANOVA and post-hoc Sheffe – test revealed an interesting pattern in executive function tests: in the Stroop and in the BADS tasks the right frontal group had a reliably impaired performance relative to the other groups, $F(4, 45) = 2.67$, $p < .05$ and $F(4, 45) = 3.89$, p < .01, respectively. In Doors and People Test all patient groups showed impaired performance in comparison with the clinical control group, F (4, 45) = 3.8, p < .01. There were no differences between the groups in the Digit- span, F (4, 45) = 3.89, p > .05; Digit-Backward Span, F (4, 45) = 3.89, p> .05; Corsi Block Taping task, F (4, 45) = 3.89, p >.05; Shifting cost of plus/ minus task, F (4, 45) = .62, p >.05, and Raven test, F (4, 45) = 3.89, p > .05.

In the next step of the statistical analysis we computed three separate executive indices: the Shifting Index, the Inhibition Index and the Updating Index.

The Shifting Index was calculated according to the following formula: Shifting Index = [Mean (Hits of List +, Hits of List-) – Hits of List +/-] / Mean (Hits of List +, Hits of List). The Inhibition Index was calculated using the following formula: Inhibition Index = (Errors from color naming condition – Errors from interference condition) / Errors from color naming condition. We calculated the Updating Index: Updating Index = [7 - (7 – Digit Backward span)] / 7. Mean values of these three executive indices vary between 1 and 0 with a score of 0 indicating disrupted executive functioning and a score of 1 effective executive functions. We have compared the performances of control and brain-injured groups, and we found significant differences only in Inhibition index, F (4, 45) = 2.67, p < .05 (see Figure 4.4). Differences in Shifting and Updating function were not found significant, F (4, 45) = .41, p > .05 and F (4, 45) = .22, p > .05, respectively. Post hoc Sheffe tests revealed that the right frontal group showed disrupted inhibition in comparision with the other groups.

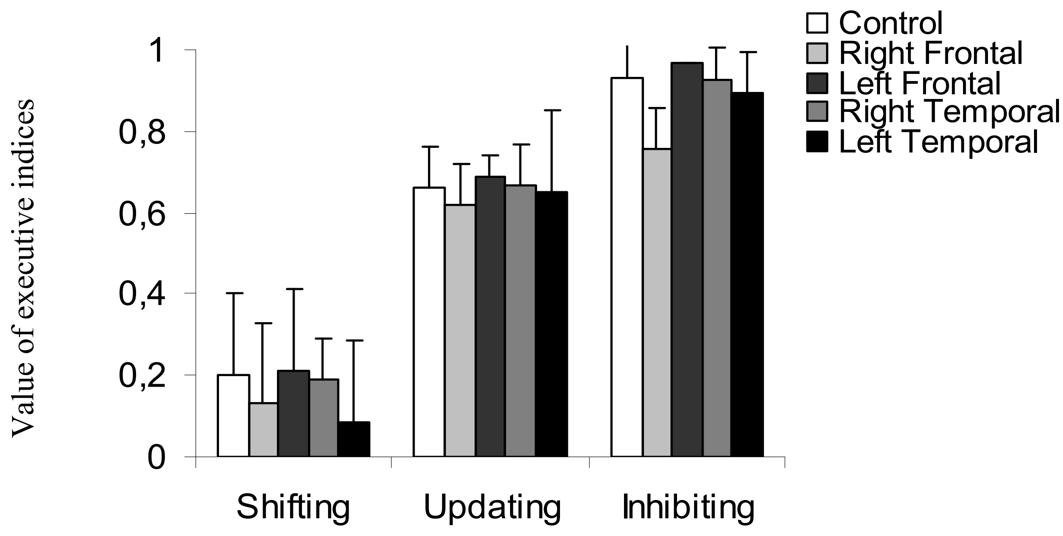


Figure 4. 4. Shifting-, Updating and Inhibition- indices. Mean values of these executive indices vary between 1 and 0 with a score of 0 indicating disrupted executive functioning and a score of 1 efficient executive functions. Error bars indicate standard deviations.

4. 3. 2. 2. Correlational results

The next step of the statistical analysis aimed to examine the relation between the different executive components and episodic memory functions. Simple tasks were selected to tap each of these executive functions: for testing Shifting function we used the shifting cost from the plus-minus tasks; the Digit-backward span was used as the indicator of the Updating factor; and finally the Inhibition factor was measured with the number of errors in the interference condition of the Stroop task (see Table 4. 6).

After establishing some separability of the three target executive functions (i.e., Shifting, Updating, and Inhibition) with no correlation between them, we examined the extent to which these functions contribute to performance on the ten episodic retrieval tasks by performing correlational studies between episodic memory tasks and executive components indicator.

As it can be seen in the Table 4.7, the Shifting factor showed significant correlation only with the CCR visual task ($r = .45$, $p < .05$). The Updating factor exhibited significant correlations with several memory tasks: SCR verbal ($r = .45$, $p < .05$), SCR visual ($r = .41$, $p < .05$) and CRN verbal ($r = .34$, $p < .05$). Although the Updating factor was considered in the original model of Miyake et al. (2000) as implicating refreshing and monitoring ability, the correlational study showed correlation with only one memory task activating monitoring funtions, the CRN verbal task. With other monitoring tasks no significant correlations were found in this case. Furthermore it seems that the Updating factor is more related to the Production factor of the hypothesis of Cabeza et al. (2003) than to the Monitoring factor. Finally, the Inhibition factor was correlated with memory tasks implicating monitoring functions, like IRN verbal ($r = .56$, $p < .01$) and IRN visual task ($r = .41$, $p < .05$), but also showed correlation with the SCR verbal task ($r = .43$, $p < .05$). ACR visual, ACR verbal, CCR verbal and CRN visual tasks exhibited no significant correlations with any of the three executive factors.

In order to examine the supposedly different executive load of episodic memory tasks and their relation to clinically used neuropsychological tests, a correlational study was performed between experimentally developed episodic memory tasks and neuropsychological tests measuring executive functions (BADS, Stroop color naming task). The overall score of the BADS test showed significant correlation with the ACR visual ($r = .49$, $p < .01$), CRN visual ($r = .49$, $p < .01$), IRN visual tasks ($r = .49$, $p < .01$) and with the merged Monitoring factor consisting of the mean recognition rate of IRN verbal, IRN visual, CRN verbal and CRN visual tasks ($r = .41$, $p < .05$), while the Stroop task was correlated with IRN verbal ($r = .56$, $p < .01$), IRN visual ($r = .41$, $p < .05$) and SCR verbal tasks ($r = .43$, $p < .05$).

Table 4. 7. Correlation of executive indices and executive tasks with the 10 episodic memory tasks

		Shifting	Inhibiting	Updating	BADS	Stroop-task
Production	ACR verbal	.04	-.16	.27	.03	.16
	ACR visual	.26	-.13	.33	**.49**	.13
	SCR verbal	.16	**-.43**	**.46**	.05	**.43**
	SCR visual	.12	-.26	**.41**	.07	.26
	CCR verbal	-.09	.29	-.09	.34	.29
	CCR visual	**.45**	-.03	-.04	**.49**	.03
Monitoring	CRN verbal	.29	-.31	**.34**	.19	.31
	CRN visual	-.22	.22	.11	-.08	.22
	IRN verbal	.13	**-.56**	.02	.21	**.56**
	IRN visual	.37	**-.42**	.30	**.49**	**.41**

Note: Significant correlation ($p < .05$) are highligted. ACR: Associative-cued recall; SCR: Stem-cued recall; CRN: Context recognition; CCR: Context-cued recall; IRN: Item recognition.

Summarizing the results of correlational studies between executive functions and episodic memory tasks it should be emphasized that different executive processes have their separate and specific roles in episodic memory tasks, and that these memory tasks are differentially related to the clinically used neuropsychological tests.

Furthermore, sustaining the „production-monitoring" hypothesis, the correlational analysis yielded results that generation of memory cues, measured by SCR tasks, was correaleted with the Updating factor. In SCR tasks the systematic memory cues generation processes are more activated than in the other tasks. Similarly, the „production-monitoring" hypothesis postulated these tasks as involving more production than monitoring processes. The Updating factor was considered in the original model of Miyake et al. (2000) as implicating refreshing and monitoring ability, but our correlational study showed correlation with only one memory task activating monitoring functions, the CRN verbal task, while with other monitoring tasks no significant correlations were found. Furthermore it seems that the Updating factor is more related to the Production factor of the hypothesis of Cabeza et al. (2003) than to the Monitoring factor. Tasks measuring the Monitoring factor from the model of Cabeza et al. (2003), like CRN and IRN tasks, were found to be related to strategic memory retrieval, including monitoring and systematic search between automatically activated memory traces. Finally, the memory inhibition process was found to be partially related to monitoring tasks not requiring monitoring the contextual features, like IRN tasks.

These correlational results suggest that possible new executive factors, like Production, and Monitoring should be taken in consideration in the executive model of episodic memory retrieval.

4. 4. General Discussion

The main goal of this section was to examine how the executive functions contribute to the performance on episodic memory- and on more complex executive tasks. In the memory domain, the executive processes are particularly involved in working memory, metamemory, generation of memory cues, monitoring contextual features, strategic memory retrieval and memory inhibition. These executive functions were differentially tested by using newly developed memory tests, classical neuropsychological tests and experimentally developed executive and episodic memory tasks. The executive components model of Miyake et al. (2000), and the production-monitoring hypothesis (Cabeza et al., 2003) were used in several correlational studies to examine the supposedly different executive load of episodic memory tasks and its relation with the clinically used neuropsychological tests.

The results yielded evidence for separate and specific roles of different executive processes in episodic memory tasks. Results of the neuropychological tests, and comparision of performance of patients with right- and left frontal and non-frontal injury across these neuropsychological tests are summarized in Table 4. 8.

Overall, the results of neuropsychological tests indicated that all patient groups had some sort of memory problems causing impaired performance in episodic memory tests (RBMT, Doors & PeopleTest, The 7 Courses Memory Test), but their general intelectual function, tested with Raven Progressive Matrices, was intact. The right non-frontal group showed impaired performance in Corsi Blocks Taping task, testing for Visuo-spatial component of WM and in visuo-spatial episodic memory (The 7 Courses Memory Test). More importantly, the right frontal group exhibited impaired performance in the tests measuring executive functions (BADS, Stroop-task, executive indices of The 7 Courses Memory Test) and the central executive (CE) component of WM (n-back, Digit backward span). In this latter test, beside the right frontal group, the left frontal group also showed impairment, indicating that CE is dependent on the bifrontal cortex, while executive tests used in these studies are loaded with executive components primarily dependent on right frontal cortex.

Table 4. 8. Performance impairment of brain injured groups in different neuropsychological tests

	Right Frontal lesion group	Left Frontal lesion group	Right non-Frontal lesion group	Left non-Frontal lesion group
Working memory tests				
Digit Span	-	-	-	-
Corsi Blocks Span	-	-	+	-
Digit-Backward Span	+	+	-	-
n-back	+	-	-	-
Episodic memory tests				
RBMT	+	+	+	+
Doors & People	+	+	+	+
7 Courses	++	+	++	+
Executive function tests				
BADS	++	-	-	-
Stroop -task	++	-	-	-
Intelligence test				
Raven SPM	-	-	-	-

Note: - indicating no impairment, + indicating impaired performance*,* ++ indicating severe impairment. RBMT: Rivermead Behavioral Memory Test, BADS: Behavioral Assesment of the Dysexecutive Syndrome, Raven SPM: Raven Standard Progressive Matrices

Correlation analysis revealed possible relations between the different executive indices measured with neuropsychological tests and experimental executive memory tasks. Several larger scale correlational studies were carried out using patients with different lesion-lateralizations and localizations, who were also likely to have a range of executive problems.

Five separable executive processes –Inhibition, Updating, Shifting, Monitoring and Production- were isolated and a higher correlation was found across the different tasks that were assumed to measure the same process with clear separation from other clusters of postulated executive processes. Table 4.9 presents the five executive components and summarizes their correlations with other executive- and memory tests and experimental tasks.

Table 4. 9. Executive components in executive- and memory tasks revealed by correlational analysis

Inhibition	Updating	Shifting	Monitoring	Production
7Courses Inhibition I.	Stroop RT Interf.I	Go/no-go RT	7Courses Self-monitoring I.	
DF cost	SCR-verbal	CCR visual	BADS	
Stroop Error Interf.	SCR-visual		IRN verbal	
IRN verbal	CRN-verbal		IRN visual	
IRN visual			CRN visual	
SCR verbal			CCR verbal	
			SCR verbal	
			ACR verbal	
			ACR visual	

Note: I: Index; DF: Directed Forgetting; Interf.: Interference; RT: Reaction Time; ACR: Associative-cued recall; SCR: Stem-cued recall; CRN: Context recognition; CCR: Context-cued recall.

It can be seen from Table 4. 9 that the Inhibition component was correlated with the DF cost and the Stroop Error Interference indices. The PCA analysis on specific error types in The 7 Courses Memory Test revealed that the Inhibition Index is a major component beside the Self-Monitoring Index. All of these inhibition measures were impaired after right frontal lobe injuries. Similarly, the performances in tasks correlating with the Monitoring component (7 Courses Self-monitoring Index, BADS, IRN verbal and visual, CRN visual, CCR verbal, SCR verbal, ACR verbal and visual) showed impairment after right frontal cortex injury. Tasks measuring the Monitoring factor from the model of Cabeza et al. (2003), like the CRN and IRN tasks, were found to be related to strategic memory retrieval, including monitoring and systematic search between automatically activated memory traces. Thus, it can be concluded that Inhibition and Monitoring are separate components with both of them depending on the right frontal cortex functioning. However, the neurological basis of the Updating and Shifting factors is not yet clear. It seems that both of these two factors are dependent on bifrontal regions, since patients with left –and right frontal lobe injuries exhibited impairments in the tasks correlating with the Updating (Stroop RT Interference Index, SCR verbal and visual, CRN verbal) and Shifting (go/no-go RT and CCR visual) components.

The present manipulations of the executive demand in episodic and working memory suggest a high degree of differential functional organization among the recruited executive control components as well as other non-executive task components. As such, our results provide empirical support for those theoretical models of executive functions that posit both unity and diversity among the executive control processes (Miyake et al., 2000; Friedman & Miyake, 2004).

5. Summary and Conclusions: Toward an integrative theory of executive processes

Despite the enormous number of studies, the concept of the executive function remains elusive. Studies in this thesis started from one basic assumption: there is no unitary frontal lobe process, there are no unitary executive functions. Rather, the different regions of the frontal lobes give rise to multiple interacting processes, and these executive subprocesses are considered to be domain general in the sense that they play an important role in a broad range of distinct cognitive domains (e.g., attention, working memory, episodic long-term memory). In the memory domain, the executive processes are particularly involved in working memory, metamemory, generation of memory cues, monitoring contextual features like temporal order, strategic memory retrieval and memory inhibition (reviewed by Shimamura, 1995).

5.1. Distinct inhibitional processes of the executive system

The first executive component, investigated in Section 2, was inhibition. An influential recent theory by Aaron et al. (2004) points to the right inferior frontal cortex as the center of the inhibitory executive system. In Section 2 we aimed to investigate the role of the prefrontal cortex and the influence of emotions on the inhibitory control processes. We selected four widely used experimental tasks that, assumingly involve inhibitory processes. The four tasks were the Stroop task, the go/ no- go task, the directed forgetting task (list method), and the selective retrieval practice task for retrieval induced forgetting effect.

According to our results from *Section 2.1,* the patients with right frontal lesion produced no inhibitory effect on the Stroop task, while the other patient group produced larger inhibitory effects compared to the right-frontal patients, although this effects in left frontal group were attenuated compared to the healthy control group. This finding is in line with with previous studies demonstrating a higher interference effect in frontal lobe injured persons, but in our study this sensitivity to interference could be observed especially in frontal patients with right lateralization.

Results from *Section 2. 2* provide similar evidence using the go/ no- go paradigm: patients with right frontal lesion showed no inhibitory effect, while other patient groups produced task-required inhibition. The right frontal group, due to the impaired inhibitory motor control, first produced false alarms and after a while by learning the goal stimuli showed “only” a higher RT.

According to results from *Section 2.3,* patients with right frontal lesion produced a reversed inhibitory effect on the intentional forgetting task. Left-frontal patients produced larger inhibitory effects compared to the right-frontal patients, although these effects were attenuated compared to the healthy control group. Finally, the patient group with temporal lobe lesion produced a comparable to normal level of inhibition, whereas lateralization of the lesion had no effect on the results.

However, results from the *Section 2.4* were somehow different: all patient groups, even the right frontal group, produced a normal level of retrieval induced forgetting.

These striking dissociations between- and within-group have several implications. Most compellingly they suggest that the Stroop-task, go/ no- go taks, DF and RIF may involve different inhibitory processes or, alternatively may involve different ways of initiating inhibition. We believe that the latter is the case and that it is the way in which inhibition is triggered that differs. In the first three, inhibitions are intentionally triggered involving active thought avoidance, while in RIF, inhibition occurs automatically and does not require any intentional thought.

In *Section 2.5* we have investigated the effects of anxiety related emotions on the inhibititory executive system by using the emotional Stroop paradigms with frontal lobe injury and with persons with generalized anxiety disorder (GAD). The data demonstrated that both frontal lobes injured and GAD groups have difficulties in inhibiting the irrelevant information, but in GAD group this effect was selective toward anxiety-related words.

Similarly, results from *Section 2. 6* provide evidence that GAD patients similarly to frontal lobe injured persons have an intentional memory inhibition bias which is selective toward anxiety related stimuli, showing no intentional forgetting effect when the words designated 'to-be-forgotten' were emotionally salient.

These results support the assumption that the right frontal cortex has a fundamental role in intentional inhibitory processes, and that these inhibitory processes can be disrupted by interfering anxiety related emotions.

5. 2. Lateralized memory-retrieval - lateralized executive processes?

A major question concearning the neural basis of the executive system is that of the separate roles of the two hemispheres in executive processes and in episodic memory retrieval. Thus the main purpose of the lesion study from *Section 3* was to examine the role of the two hemispheres in the different executive and memory processes. This lesion study was designed to contrast the current hypotheses about the role of the two hemispheres in episodic retrieval processes. Classical neuropsychological studies provide evidence for material-specifity. Whereas the well known hemispheric encoding/ retrieval asymmetry (HERA) model emphasizes the role of the left hemisphere in encoding, the right hemisphere has been considered to be more active during episodic retrieval. The "systematic – heuristic" hypothesis states that the left PFC is more involved in systematic retrieval, while the right PFC is more active in heuristic retrieval. The "production- monitoring" hypothesis proposes that the left PFC is primary involved in semantically guided production of information, while the right PFC is more active during monitoring processes. Involving frontal and temporal lobe patients with left or right-sided lesions, we used ten different verbal and visual recall and recognition tasks loading different processes of production and monitoring, and also of analytical and heuristic processes. Thus, the results support the assumption that the "production- monitoring" hypothesis is more appropriate in explaining the effect of frontal lobe lesions on memory performances, while the heuristic-systematic hypothesis is more suited to explain the effect of temporal lobe lesions on episodic memory.

The result of PCA analysis performed on experimental tasks gave evidence of four factors: two of them, the Monitoring and Production factors were similiar to the two main factors postulated by the model of Cabeza et al (2003). Besides monitoring and production processes, the other two factor, namely the Contextual memory and Familiarity effect may have an important role in memory retrieval as separate factors. These results fit very well the idea that the right PFC is more involved in monitoring operations, including the evaluation and verification of recalled information, whereas the left PFC is more involved in semantically guided information production processes (Cabeza et al., 2003).

The main conclusion to be drawn from Section 3 is that the monitoring processes are related to the right prefrontal cortex while the production process is more dependent on left prefrontal functioning, and these two factors can be considered as separate executive functions.

5. 3. An integrative theory of executive processes

Recent models have suggested a view of the executive functions as a conglomerate of largely independent, but interacting control processes such as interference resolution, attention-shifting, updating, and inhibition (Johnson, 1992; Baddeley, 1996; Fuster, 1997; Smith & Jonides, 1999; Miyake et al., 2000; Friedman & Miyake, 2004; Marklund et al., 2007). In studies from Section 2 and Section 3 we have investigated the inhibition, monitoring and production components of the executive system, while in Section 4 we aimed to examine the relations between the different executive components, trying to find common components in classic neuropsychological tests and in newly developed, experimental memory and executive tasks. The executive components model of Miyake et al. (2000), and the production/ monitoring factors (Cabeza et al., 2003) were used in several clinical and correlational studies to examine the supposedly different executive load of episodic memory tasks and its relation to the clinically used neuropsychological tests.

The results yielded evidence for the existence of separate and specific roles of the different executive processes in episodic memory tasks. First, we identified some of the executive processes and marshalled evidence for their relationship to specific frontal regions. Five clearly separable executive processes were defined with correlation and PCA analyses: Inhibition, Updating, Shifting, Monitoring and Production (strategy generation).

Summarizing the results (Section 2 – Section. 4), they provide evidence for an anatomically and functionally discrete cognitive architecture of the frontal lobes (see Table 5.1). We moved from a comparision of the frontal versus posterior lesions to the standard anatomical classification within the frontal lobes: right frontal, left frontal, and bifrontal. However, it should be noted, that at this stage, the architecture is yet an unfinished structure. As it can be seen from Table 5.1, two components of our executive model are dependent on right frontal lobe functioning: the Inhibition and Monitoring components. These two components were extensively studied in Section 2, Section 3 and Section 4.1. Studies from these sections provided clear evidence for the role of the right prefrontal cortex in intentional inhibition and in monitoring processes. The other three components – Updating, Shifting and Production- were not as meticulously studied as Monitoring and Inhibition, but studies from Section 3 and Section 4 provided evidence for the left frontal involvement in the Production factor (Section 3), and for the role of bifrontal areas in the Shifting and Updating factors (Section 4).

Table 5. 1. Distinct executive components and their neurological basis

	Inhibition	Monitoring	Shifting	Updating	Production
	Right Frontal Cortex		***Bifrontal Cortex***		***Left Frontal Cortex***
Section 2.1.	Stroop Error Interf.I.			Stroop RT Interf.I	
Section 2.2.	Go/no-go RT				
Section 2.3.	DF cost				
Section 3.		IRN-verbal IRN-visual CRN-visual CRN-verbal CCR-verbal ACR-verbal ACR-visual			SCR-verbal SCR-visual ACR-verbal ACR-visual
Section 4.1.	7Courses Inhibition I.	7Courses Self-monitoring			
Section 4.2.	Stroop Error Interf.I.	BADS	BADS-I	n-back	
Section 4.3.			+/- task CCR-visual	Digitbackward SCR-verbal SCR-visual CRN-verbal	

Note: I: Index; DF: Directed Forgetting; Interf.: Interference; RT: Reaction Time; ACR: Associative-cued recall; SCR: Stem-cued recall; IRN: Item recognition; CRN: Context recognition; CCR: Context-cued recall.

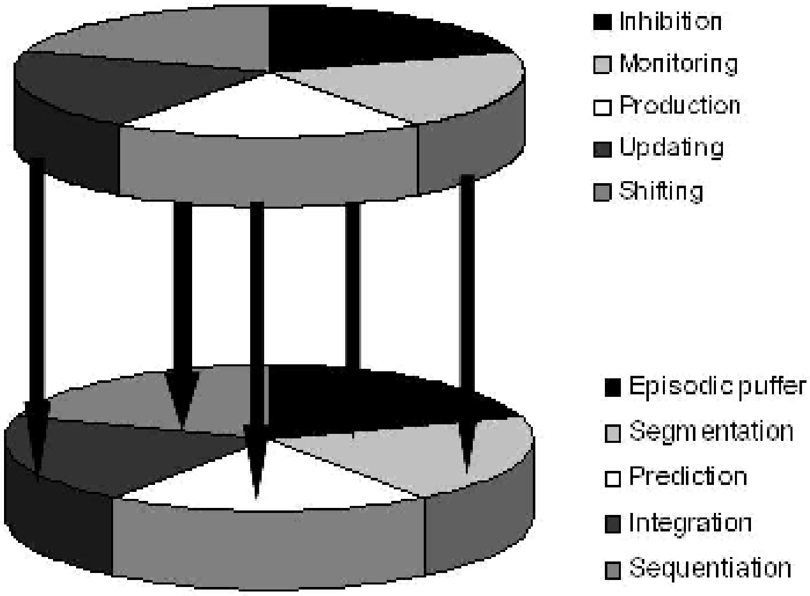
This analysis should be regarded as a preliminary attempt to separate processes within tasks using this method. The necessary next step is to cross validate the patterns identified here in a larger sample of patients to determine the stablity of these findings. The eventual goal would be to identify the unique covariance across measures that represent neuropsychological dimensions represented to varying degrees in their relation to lesion location.

5. 4. Future directions

The integrative executive model presented above is based on researches providing evidence for the non-unitary, constantly interacting executive processeses, which are considered to be domain-general in the sense that the subprocesses play an important role in a broad range of distinct cognitive domains. We used different neuropsychological tests and experimental tasks to prove this domain-generality of the executive subprocesses. In this final section we shall try to give a theoretical example of the domain-generality of our integrative executive model. Since the aim of this thesis was to examine the lateralized executive subprocesses during episodic memory retrieval, we use for this demonstration the Grafman (2002) model of episodic memory system which is postulated to be dependent on PFC functions. Grafman argues that the human PFC stores a unique type of knowledge in the form of structured event complexes (SECs) (Grafman, 2002). SECs are representations composed of higher-order goal-oriented sequences of events that are involved in the planning and monitoring of complex behavior (Grafman, 1995; 2002). The PFC processes goal-oriented SECs by encoding and retrieving the sequence of the event components. Specifically, event components interact with each other and give rise to event sequence knowledge through three binding mechanisms: (1) sequential binding for linking event components within the PFC; (2) segmentation and temporal binding for linking event components with anatomically densely connected regions in the posterior cortex; (3) integration of event components with anatomically loosely connected regions through synchronized activity induced by the hippocampus. Beside sequentiation, segmentation and integration components, a prediction component and the episodic puffer component from the new WM model of Baddeley (2000) form together the episodic system model proposed by Grafman (1995, 2002).

These five components fit well with our five components: Shifting, Monitoring, Inhibition, Production and Updating (see Figure 5.1, after Racsmány, 2008). The episodic puffer implements inhibition functions, while prediction is related to production, generating new strategies and cues. Sequentiating is dependent on the shifting functions and segmentation is related to the monitoring abilities. Finally, for the integration of new information, the updating function is required. At this stage, the comparision of the two models is still an ongoing process, altough these two models seem to be compatible. However, it should be emphasised that this is only an attempt for the integration of different models and a possible suggestion for further research.

Executive components



Components of episodic system

Figure 5.1. The relationship between the executive subprocesses of our executive model and the components of the episodic system model of Grafman (2002; Racsmány, 2008). The episodic puffer implements inhibition functions, segmentation is dependent on monitoring abilities, prediction is related to production, while for the integration of new information updating function is needed. Sequentiating is related to shifting functions.

Activation studies with neurologically intact individuals using functional magnetic resonance imaging (fMRI) and positron emission tomography (PET) also indicate that multiple regions are active during the performance of a specific task and identify how distinct frontal brain regions are related to a particular element of the executive processes. However, such studies cannot normally differentiate all the different processes required for a complex task, since PET and fMRI are used to average results over time. Lesion research, by identifying that damage to a specific brain region impairs a relatively unique function, provides additional information related to the notion that specific brain areas are responsible for specific functions. In addition, functional imaging that provides temporal analysis, such as event-related potentials (ERP) or magnetoencephalography (MEG), combined with source localization, would be in vivo on-line method differentiating various processes related to different brain localizations. Newer methods of analysis of the activation paradigms may disentangle the supportive and the essential elements of various brain networks activated by specific executive processes. However, this leads on to a further question of how the component sub-processes are related to each other.

Summarizing the findings from the previous sections, we tried to put forward a possible integrative-executive model, but wished to leave open to empirical investigation the question whether the organization is hierarchical with one or more subsystems dominating, or whether a more heterarchical structure is involved. Nonetheless, since lesion studies indicate which regions are necessary for a function, our results may provide a framework for more localized patient and imaging studies in the future.

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