Chapter 1

Executive Functioning: Rehabilitation after Brain Injury and the Contribution of Functional Neuroimaging.

Executive functions[1]

Executive functions (EF) are higher cerebral functions controlled by frontal lobe systems that enable a person to intentionally initiate and regulate new patterns of behaviour and ways of thinking, and to introspect upon them. They are involved in a whole range of adaptive abilities and behaviours which are required most in novel, non-routine situations or in situations where the usually performed, routine behaviour is no longer useful or appropriate.

Norman and Shallice (1986) developed a model which clarifies the role and position of these 'frontal functions'. It is based on two main premises. The first is that routine selection of routine actions or thought operations is decentralised. This they termed 'contention scheduling'. The second assumption is that non-routine selection is qualitatively different and involves a general-purpose Supervisory Attentional System (SAS) which modulates rather than dictates the rest of the system. This model implies that in routine situations there is an automatic selection of an appropriate schema. The result of this selection process is dependent on the context and content of the stimulus situation. In new situations when tasks can not be performed routinely the SAS is activated. It does not directly select the schema to be used, but influences the process of activation of certain schemata. Norman and Shallice describe attention as the factor which controls activation and inhibition and assume that motivational factors supplement the activational influences of the SAS. Shallice (1988) summarises the role of the SAS as follows:

> ... the Supervisory System [has] access to a representation of the environment and of the organism's intentions and cognitive capacities. It is held to operate not by directly controlling behaviour, but by modulating the lower level [resources] by activating or inhibiting particular schemata. It would be involved in the genesis of willed actions and required in situations where the routine selection of actions was unsatisfactory - for instance, in dealing with novelty, in decision making, in overcoming temptation, or in dealing with danger. (Shallice, 1988, p335)

[1] The terminology of the International Classification of Functioning, Disability and Health (ICF; World Health Organization, 2001) is used. The word 'function' refers to physiological functions of body systems, including psychological functions. 'Functioning' is broader and additionally includes the activities people do and their participation in certain life areas.

On the behavioural level EF have been conceptualised into four different components: volition, planning, purposive action, and effective performance (Lezak, Howieson, & Loring, 2004). The term volition is used to describe the 'capacity for intentional behaviour' and is essential in the other three components. Planning involves the organisation of the steps and elements needed to achieve a goal. This requires the ability to anticipate, to have an objective view on oneself and one's environment, and to consider alternative behaviour (Lezak et al., 2004). Besides planning a task, its execution is an essential step in purposeful behaviour. In order to execute a task, the actor has to initiate a particular plan while simultaneously ignoring irrelevant or competing needs, wants, or other plans. To ensure effective performance, the ongoing action is constantly monitored and compared with the original plan. If necessary the actor stops, self-corrects, and consequently switches flexibly to other behaviour. This regulation of behaviour implies that a person is able to keep his or her intentions active in working memory over a long period of time without external cueing. Next to that he or she must recognise errors and be motivated or able to correct possible errors. As soon as the desired goal has been achieved, the actor has to recognise this and terminate his or her actions. Ylvisaker (1998) suggests another classification which clarifies the role of executive functioning in daily life activities: *self-awareness* of strengths and needs; realistic and concrete *goal setting; planning and organizing* the steps to these goals; *self-initiating* these plans; *self-monitoring* and evaluating performance according to plan and goal; *self-inhibiting* behaviour that does not lead to the goals set; *flexibility and problem solving* when situations can not be dealt with according to plan; and *strategic behaviour,* that is generalisation of successful behaviours to other situations. A situation in which the above is brought into practice is best described as 'multitasking' (Burgess & Simons, 2005a). The authors distinguish this from multiple-task performance by stating that multitasking involves an ill-structured situation and the activation of delayed intentions.

Essentially, EF should not be reduced to 'cold' cognitive components leaving out the clinically essential aspects of self-monitoring, initiative and 'hot' cognition (emotional evaluation and mental effort). Through these aspects, EF play a critical part in complex social behaviour. Barkley (2001) puts it even stronger by stating that the ultimate purpose of EF is to maximize the social outcomes for the individual. A cognitive framework for understanding these prefrontal dynamics is provided in figure 1 (Brouwer & Schmidt, 2003).

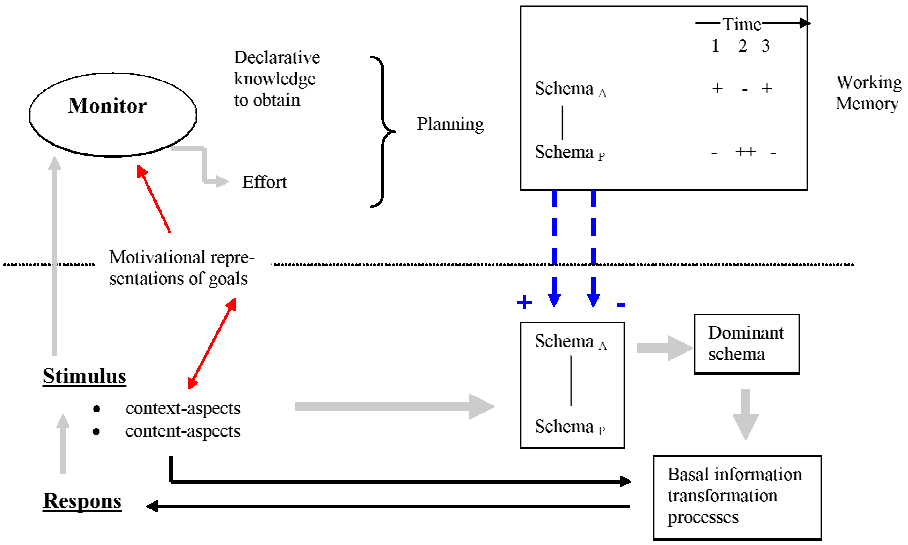

Figure 1. Revised mental schema theory (Brouwer et al., 2003)

This model is a supplement to the Norman and Shallice model. Above the horizontal dotted line psychological processes are indicated that are representative for EF. Below the dotted line implicit automatic aspects of information processing and memory are indicated: contention scheduling. SAS control of schema-driven information processing is activated if a discrepancy between actual and required goal attainment is sensed. This framework complements the other model by adding the awareness of own (dys)functioning (the monitor), which plays a critical role in activating the SAS, but certainly is not equivalent to it. This awareness of own performance is a very important but often neglected aspect of executive functioning. The model illustrates that executive dysfunctioning not only can lead to practical problems; it can also cause problems or misunderstanding in social situations. We can conclude that EF play an important role in independent functioning in daily life, also in social situations, and as a result, in the quality of life a person experiences.

After defining EF on the behavioural level, the question arises where these functions are to be found anatomically. However, localisation of EF is a complex matter. Though they are often referred to as "frontal lobe functions" and the (pre)frontal lobe plays a central role, EF are the result of neural processing without a specified location, either in the frontal cortex or elsewhere. This idea is elaborated by Elliott (2003) who describes executive functioning as being mediated by dynamic and flexible networks. She states that executive functioning does not depend on the prefrontal cortex in isolation, but on an intact corticostriatal circuitry mediated by dopaminergic neurotransmission. Linking anatomy with behaviour Fuster (1997) explains:

> Behavioural actions are represented in relatively segregated domains of the cortex of the frontal lobe…. Each is hierarchically organized. Within it, actions are represented by increasing order of complexity and novelty in successively higher and interconnected areas. Actions that have become automatic and routine are represented in lower levels of motor hierarchies…. All action domains extend forward into the prefrontal cortex, where the more complex and novel actions are represented…. The decision to undertake a course of action is a multidetermined phenomenon, a vector of numerous and diverse neural influences that from other brain regions converge at a given time on the frontal cortex. Foremost among these influences are the basic drive and motivations of the organism, which arrive in frontal cortex from diencephalic and limbic formations. Other inputs arrive from sensory receptors and areas of posterior (perceptual) cortex. (Fuster, 1997, p250-251)

When ultimately trying to locate the different behavioural components of executive functioning, the prefrontal cortex can be subdivided into three regions (e.g. Cummings, 1995; Sbordone, 2000; Stuss & Benson, 1984): the dorsolateral prefrontal cortex is mostly active in planning and purposive action; the medial frontal cortex participates in motivation, drive and initiative; and the orbitofrontal cortex is involved in emotional and social behaviour. In figure 1 these components mainly come into play in the SAS activities located above the dotted line: planning, motivation and effort, and monitoring of emotional and social consequences of situations. However, emotional and motivational states can also play an important role in automatic schema selection, in their quality of internal context factors. Knowledge of the diverse components that constitute executive functioning and how they are linked to each other at these different levels is essential in order to successfully diagnose and treat executive functioning problems.

Dysexecutive syndrome

Executive dysfunctioning, or a dysexecutive syndrome, can have various neurological and psychiatric causes, either as a result of lesions in the frontal-cortical-subcortical circuits or alterations of metabolic activity of these circuits. Though the dysexecutive syndrome can arise irrespective of aetiology or localisation of the damage this does not imply that any type of brain injury can lead to executive dysfunctioning: the frontal cortex has to be directly affected or indirectly, due to lesions elsewhere in the circuitry. Whether and which specific executive

dysfunctions become apparent and how severely they affect a patient's life differs due to variability in premorbid characteristics, aetiology, and localisation of the brain injury. The diverse behavioural manifestations of the dysexecutive syndrome can be made clear using the Norman and Shallice model and the revised mental schema theory (figure 1) both discussed above. When the SAS is not operating as it should, selection of behaviour will be done routinely. This will especially give problems in situations that are novel and complex, for instance, when an unusual response for a certain context is required. Typically, the dysexecutive syndrome results in one or more of the following: reduced awareness of impairments or a non-realistic approach to them; disorganised planning of actions; reduced initiative; disorganised regulation of actions; inappropriate or uninhibited social behaviour; rigidity of behaviour; or inability to generalise to other situations.

In the clinical practice of rehabilitation there are two main aetiologies underlying the dysexecutive syndrome: stroke and traumatic brain injury. TBI typically is diffuse axonal injury. In the more severe cases it is accompanied by more localised damage, often fronto-temporal. Therefore, a large part of the people suffering TBI will experience executive functioning problems (e.g. Satish, Streufert, & Eslinger, 2006; Ylvisaker & Feeney, 1996). Those problems may still be present many years post-injury (Ponsford, Draper, & Schönberger, 2008; Spikman, Deelman, & Zomeren van, 2000a). Deficits in Lezak's planning component, appear to be an important underpinning of the impairment of everyday living activities after TBI (Fortin, Godbout, & Braun, 2003). Also purposive action and effective performance have been found impaired (McDonald, Flashman, & Saykin, 2002; Spikman et al., 2000a). Spikman et al. (2000a) further concluded that patients with specifically focal frontal damage were especially impaired and that, as a result, they had to rely more heavily on externally provided cues. In a clinical study (Pachalska M., Kurzbauer H., Talar J., & MacQueen B.D., 2002), the consequences of TBI on a behavioural level were subdivided in an active (acting without thinking: impulsiveness) and a passive (thinking without acting: reduced initiative) form of the dysexecutive syndrome; disorders in planning and volition, respectively. Both forms will, of course, only be seen as a disorder when they lead to maladaptive behaviour. In routine situations acting without thinking can be very useful and timesaving. Thinking without acting should perhaps be done more by some people who quickly turn to aggressive behaviour. In recent years the 'hot' aspects of executive functioning have also become subject of study. According to Spikman (2003) there is increasing evidence that social attention ("the ability to observe and interpret social situations correctly, whereby social situation refers to any interaction with another human being" (p. 173)

can be impaired in TBI. Hornak, Rolls and Wade(1996) observed socially inappropriate behaviour in a group consisting of both TBI and stroke patients with ventral frontal lobe damage who suffered from impairments in the identification of facial and vocal emotional expression. In a study on TBI patients with frontal lesions, deficits in social cognition were found that were not related to results on measures of 'cold' executive functioning. The authors suggest that both hot and cold aspects of executive functioning can be variably impaired (Spikman, Veenstra, van der Naalt, Milders, & Brouwer, 2005). The ability to make inferences about another's mental state (so-called "Theory of Mind") also has been found to be impaired in TBI and stroke patients (Milders, Fuchs, & Crawford, 2003; Stone, Baron-Cohen, & Knight, 1998).

In stroke patients there has been less extensive research on the dysexecutive syndrome. The research done suggests that it is quite common after stroke (eg Ballard et al., 2003; Vataja et al., 2003) and, like in TBI, can differ in each patient in the symptoms that manifest themselves. Effective performance and purposive action have been found impaired. (Ballard et al., 2003; Leskela et al., 1999; Vataja et al., 2003) . Finally, also in stroke patients there is increasingly more attention for the possibility of changes in social/emotional behaviour. Brodaty (2005) found that apathy is common after stroke and that its presence may be related to older age and right fronto-subcortical pathway pathology, rather than stroke severity. The type and location of stroke is hypothesised to influence which functions will show most impairments, including behavioural/emotional self-regulatory functioning (Stuss, 2007).

Assessment of executive functioning

Neuropsychological tests

To estimate the nature and severity of the dysexecutive syndrome, neuropsychological assessment is necessary. In that assessment also other, cognitive, functions should be considered, like memory, attention or slowness of information processing. Poor performance on a certain test can be attributed to many different deficits (e.g. Rabbitt, 1997; Spikman, Timmerman, Zomeren van, & Deelman, 1999). Especially where EF are concerned it is important to have thorough information because these functions are essential in independent functioning in daily life and play an even larger role in the rehabilitation phase after brain injury. The lives of brain-injured patients suffering cognitive and physical impairments have changed and are now full of new and unstructured situations. Therefore, EF are indispensible in the process of resuming previous activities. To guide a patient best in that process, tests should result in useful information on expected executive functioning in daily life; i.e. be ecologically valid.

Ecological validity in a neuropsychological context has been defined by Sbordone (1996) as: "the functional and predictive relationship between the patient's performance on a set of neuropsychological tests and the patient's behaviour in a variety of real-world settings" (p. 16).

Regrettably though, neuropsychological tests have proven to fall short in the estimation of a person's executive functioning in daily life situations. Well known tests for EF are: the Tower of London test (ToL; Shallice, 1982), Stroop test (Stroop, 1935), Wisconsin Card Sorting test (WCST; Berg, 1948), Trailmaking test, and the Behavioural Assessment of the Dysexecutive Syndrome (BADS; Wilson, Alderman, Burgess, Emslie, & Evans, 1996). The ToL test was not sensitive in the assessment of patients with severe, diffuse, TBI (Cockburn, 1995) or patients with chronic TBI (Spikman et al., 2000a). In Demakis' study (2004) the Stroop test did not show the expected effect for frontal lobe patients. Anderson et al. (1995) found that the WCST and the Trailmaking test were not sensitive for dysfunctions in a group of TBI patients with and without frontal lobe lesions. The BADS is claimed to be an ecological valid measure able to predict executive functioning in daily life. It proved to have larger predictive value than the WCST (Wilson, 1993), but still the ecological validity of the BADS has been found to be limited in the assessment of patients with brain injury (Norris & Tate, 2000a; Wood & Liossi, 2006). In studies on the assessment of EF (e.g. Burgess, Alderman, Evans, Emslie, & Wilson, 1998; Manchester, Priestley, & Jackson, 2004), these difficulties have been confirmed: clinical instruments designed to assess EF appeared to have variable sensitivity and specificity, and only low-to-moderate ecological validity. According to Manchester et al. (2004) office-based tests of executive functioning might be of use when deciding on rehabilitation approaches, but the assessment of executive dysfunctioning in daily life is best achieved by naturalistic assessment measures combined with information about the patient's behaviour provided by significant others.

The fact that especially EF are hard to capture, is a result of the ongoing theoretical discussions as to what executive functioning is and how all its elements can be assessed (Rabbitt, 1997). Executive functioning in daily life is needed in situations where criteria for success are not clearly specified, goals must be kept active over a long period of time without externally provided structure, and interruptions have to be dealt with. Furthermore, the essence of EF is the self: self-initiation, self- structuring and self-regulation. Obviously, these elements are hard to incorporate in a standardised neuropsychological assessment. Cues, both minor and those inherent in an assessment situation (Spikman et al., 2000a), absence of distraction, and structure provided (Chamberlain, 2003) make the assessment situation quite the opposite of daily life.

Additionally, most tests only assess one or two of the many elements involved in the complex process of EF in the brain and ignore the remaining elements, particularly motivation and emotion. Related to this, EF tests may also make demands on other (non-executive) cognitive skills or functions (Rabbitt, 1997). All of this can result in brain injured patients performing on the level of healthy controls in an assessment procedure while experiencing problems in daily life (e.g. Wood & Rutterford, 2004).

The reason why so many neuropsychological tests with low ecological validity have been developed, and are still used, lies in the history of neuropsychology as well as the developmental history of the tests. Neuropsychologists primarily assisted in the diagnosis of brain pathology before they were being asked to make recommendations about a person's daily life functioning. To answer these relatively new questions, tests are used that were originally developed to answer diagnostic questions and in most cases those tests lack ecological validity (Chaytor & Schmitter-Edgecombe, 2003). Linked to this, Burgess et al. (2006b) describe, specifically for EF, the process whereby tests until now were being developed, why that approach is not likely to result in clinically useful tests, and what might be a better approach to the development of an EF test. They claim that most tests are based on a theoretical construct or cognitive resource and therefore result in information on these hypothesised resources, which is not easily translated into real-life functioning. Especially where EF are concerned, test development should be based on a function[2], or, in the authors' definition: directly observable behaviour. This is most likely to result in a test fit for clinical purposes. A "function-led" approach in test development would for instance ensure that the actual situation in which the assessment takes place is more like daily life and that more elements involved in the complex process of executive functioning are being assessed.

The lack of ecologically valid tests, has led to the development of several new tests. For example, the BADS was developed as a more ecologically valid test than the tests being used at that time. Other tests include: the Multiple Errands Test (Alderman, Burgess, Knight, & Henman, 2003; Shallice & Burgess, 1991), the Hotel Task (Manly, Hawkins, Evans, Woldt, & Robertson, 2002), and the Executive Secretarial Test (Spikman et al., 2007). This last test led to better predictions on everyday functioning than the BADS (Lamberts, Evans & Spikman, 2009a).

[2] Although ICF classification demands the use of the word "functioning" in this context, the authors' use of the word "function" has been maintained to prevent ambiguity when referring to their "function-led" approach.

Functional neuroimaging

Not only new tests have been developed, also new techniques are being used to increase understanding of executive functioning and its underlying processes. In the attempt to locate EF anatomically, functional neuroimaging techniques have become popular in neuropsychology. These techniques can be subdivided in structural and functional techniques. Structural techniques provide anatomical information and functional techniques show local changes of physiological processes in the brain. These changes are linked to neural processes and with that to activities like fist clenching, but also to cognitive and emotional activities. Functional neuroimaging itself can also be subdivided (Rossini & Pauri, 2000). One group analyses electromagnetic properties of the brain neurons, which can be assessed via modern types of ElectroEncephaloGraphy (EEG), MagnetoEncephaloGraphy (MEG) and Transcranial Magnetic Stimulation. The second group uses regional blood flow and metabolic changes as indicators of neural activation. Examples are: Positron Emission Tomography (PET), functional Magnetic Resonance Imaging (fMRI), and Functional Near-Infrared Spectroscopie (fNIRS). The last method might become more popular in future as it offers portable and low-cost monitoring of brain activity (Irani, Platek, Bunce, Ruocco, & Chute, 2007).

In the recent literature, activation patterns show overlap as well as distinctiveness in brain structures involved in different aspects of executive functioning. Planning of an action was found to be mainly located in the dorsolateral prefrontal cortex and the anterior part of the cingulate cortex (Dagher, Owen, Boecker, & Brooks, 1999; Lazeron et al., 2000). Andrés (2003) reviewed data from lesion and neuroimaging studies on purposive action and effective performance. From the neuroimaging literature she concluded that although the prefrontal cortex is importantly involved in EF, other areas, such as parietal, temporal and hippocampal areas, are also activated during the performance of EF tests. At which of these locations the activation is found, is largely determined by the test and the demands it makes on the subject. Garavan, Ross, Murphy, Roche, and Stein (2002) studied brain activation during a test requiring purposive action and effective performance. Like Andrés (2003) they found that subjects show activation in right prefrontal and parietal areas, and regions of the cingulate during inhibitory control. Error detection was found to activate the anterior cingulate and the pre-SMA. In behavioural alteration subsequent to errors the left prefrontal cortex and, again, the anterior cingulate were found active. Another study on purposive action and effective performance (Szameitat, Schubert, Müller, & von Cramon, 2002) demonstrated that the dorsolateral prefrontal and superior parietal cortices were involved. In their study on effective performance,

van Veen, Cohen, Botvinick, Stenger, and Carter (2001) concluded that the anterior cingulate cortex has a highly specific contribution to EF through the detection of conflicts occurring at later or response-related levels of processing. Sylvester et al. (2003) evaluated whether there was a single executive process or multiple executive processes working together during purposive action and effective performance. They concluded that there are common selective attention processes in which the dorsolateral prefrontal, parietal, medial frontal, and premotor cortices are involved. Different neural areas, however, carry out the actual manipulation of attended information. The authors present this as evidence for the separability of cognitive processes underlying EF. Overall, we can conclude from this selection of studies that there are a few brain structures that seem to be involved in nearly every aspect of executive functioning: the dorsolateral prefrontal cortex, the anterior cingulate cortex, and several parietal areas.

The potential of functional neuroimaging for assessing brain activation in relation to cognitive and executive tests has great interest and appeal, but researchers should be aware of the limitations and the risk of over-interpreting the results (Bub, 2000; Papanicolaou, 1999). For instance, functional neuroimaging does not guarantee that the observed brain activity is necessary for an isolated cognitive process. This is because researchers never have perfect control over the cognitive processes in which a subject engages (D'Esposito, 2000). Thus, essentially neuroimaging is an observational, correlative method (Sarter, Berntson, & Cacioppo, 1996) and results should be interpreted accordingly. A more technical problem is that of detecting effects in large vessels in addition to changes in the capillary beds that irrigate the grey matter tissue, while only the latter is related to the paradigm. An alternative to traditional BOLD fMRI that may address this issue is perfusion fMRI using arterial spin labelling (Hillary et al., 2002). In spite of these limitations, functional neuroimaging studies are providing us with new insights regarding the organisation of the cerebral cortex as well as the neural mechanisms that underlie cognition, especially when the data are combined with other methods like lesion studies (D'Esposito, 2000) or neuropsychological testing.

The use of functional neuroimaging has also increased in research on brain injured patients. In this field, these techniques can have several promising applications, for instance as a potentially useful tool in the diagnostic process. Other clinical applications include: the ability to detect abnormalities not seen on static imaging, or larger areas of dysfunction than those seen on static imaging; providing insight in processes underlying recovery of functioning (Mountz, 2003; Munoz-Cespedes, Rios-Lago, Paul, & Maestu, 2005; Scheibel et al., 2003); and expanding the knowledge about the precise processes through which the recovery takes place with the

ultimate goal of finding the best therapy for each individual patient (Azouvi, 2000; Bigler, 2001; Hillary et al., 2002; Ricker & Zafonte, 2000; Rijntjes & Weiller, 2002). In both TBI and stroke, functional neuroimaging studies have shown that there is a close link between cognitive and behavioural disorders and brain activation patterns or blood flow indices (e.g. Brodaty et al., 2005; Christodoulou et al., 2001; Fontaine, Azouvi, Remy, Bussel, & Samson, 1999; Oder et al., 1992; Turner et al., 2007). Neuroimaging can suggest alternative hypotheses where traditional methods are out of options. For instance, in brain-injured patients with complaints about their cognitive functioning that could not be objectified in neuropsychological tests. McAllister et al. (1999) hypothesised on the basis of neuroimaging findings, that they had difficulty activating or modulating task processing resources due to their injury. This would lead to normal test results while experiencing that more effort has to be put into a task than before brain injury.

However appealing these results may seem, in brain-injured populations the use of functional neuroimaging and the interpretation of results are linked with additional limitations compared to studies using healthy controls. A problem in the interpretation of data is caused by the wide variability in anatomical and functional organisation after brain injury (Hillary et al., 2002). This implies that in a study on brain-injured patients it is not possible to perform a group analysis. Furthermore, the limited knowledge of brain activity in normal and in neuropathological states, and the little there is known about the effect brain injury and related complications have on fMRI measurements (Hammeke, 1999; Hillary et al., 2002) require extra caution in designing such a study. To control the influence of these unknown factors in data interpretation as much as possible there should be meaningful relationships between imaging data and neuropsychological testing. Furthermore, cognitive activation paradigms should be used during functional imaging sessions rather than after (Ricker et al., 2000). According to Price (2002) the most significant limitation is that functional imaging with patients needs tests that the patients can perform: tests that take their physical and cognitive limitations into account. Other complicating factors in functional neuroimaging of patients with acquired brain injury can be: compliance with motion restrictions, extra time needed relative to healthy volunteers, and test compliance (Hammeke, 1999). Eventually, functional neuroimaging may become an addition to neuropsychological assessment in the diagnostics of executive functioning. That extra information could be helpful in the decision of exactly which elements of executive functioning should be treated in a specific patient and in the evaluation and subsequent improvement of treatment methods.

Rehabilitation of the dysexecutive syndrome

Recovery after brain injury can be defined at the same two levels as brain injury itself: at the level of activity limitations and participation restrictions and at the level of functional or neural impairment. After brain injury spontaneous recovery will occur to a certain degree. Additionally, experience dependent changes or changes due to rehabilitation have been found at both levels.

Neuropsychological rehabilitation

Many authors use the term 'cognitive rehabilitation' instead of 'neuropsychological rehabilitation'. According to Fasotti (2005) the term 'cognitive rehabilitation' should be used only when referring to the combination of psychoeducation, adaptations of a persons environment, and cognitive training. Cognitive training, in his definition, is aimed at minimising the impairments directly caused by cognitive dysfunctioning and learning to cope with them. Cognitive rehabilitation is part of a larger field: neuropsychological rehabilitation. This larger field includes all interventions by a neuropsychologist within the rehabilitation of neurological patients: psychosocial, behavioural, emotional and cognitive. These treatment options together with diagnostics and research belong to the field of clinical neuropsychology. Many authors use the term 'cognitive rehabilitation' when the use of either 'cognitive training' or 'neuropsychological rehabilitation' would be more correct according to Fasotti. In this chapter terminology will be translated in Fasotti's terms to make it clear which element of the field of clinical neuropsychology is being discussed.

Neuropsychological rehabilitation is recognised as an important factor aiding the process of picking up, as much as possible, life as it was before brain injury (e.g. Carney & Coudray du, 2005; Cicerone et al., 2005; Lincoln, 2005). It can be defined as a "systematic, functionally oriented service of therapeutic activities that is based on assessment and understanding of the patient's brain-behavioural deficits" (Cicerone et al., 2000, p. 1596). Prigatano (2005) adds that neuropsychological rehabilitation "refers to nonpharmacological and nonsurgical interventions by healthcare providers that aim to improve or restore problem-solving capabilities of brain function" (p. 3) that have become dysfunctional after brain injury. Furthermore, it should "help patients to manage residual neuropsychological disturbances as they emerge into interpersonal situations" (p. 3). Finally, Wilson (1989, p. 117) includes several approaches in her definition: "any intervention strategy or technique which intends to enable patients, and their family, to live

with, manage, by-pass, reduce or come to terms with cognitive deficits precipitated by injury to the brain".

According to Hillis (2005) learning theory has provided many principles on which the interventions in neuropsychological rehabilitation are based. It has made therapists incorporate errorless learning, spaced practice instead of mass practice, and random, intermittent reinforcement rather than constant reinforcement into their rehabilitation. There are various interventions in neuropsychological rehabilitation and these can be subdivided in different categories. Cicerone et al. (2000) describe the following: reinforcing, strengthening or re-establishing previously learned patterns of behaviour; learning to use compensatory, internal, cognitive mechanisms; learning to use external compensatory mechanisms; and enabling persons to adapt to their cognitive disability even though modifying or compensating for cognitive impairments are not possible. Many of the current methods involve learning patients to compensate for their deficits, although there is increasing interest in restorative approaches (Wilson, 2000). The latter have not yet proved to be effective, whereas compensation has repeatedly been demonstrated as an effective strategy (Cicerone et al., 2000; Cicerone, 2004).

Neuropsychological rehabilitation of the dysexecutive syndrome is broadly conceptualized as "shifting the individual from a more dependent, externally supported state to a more independent and self-regulated state" (Mateer, 1999, p. 50). However clear this definition is, treatment of the dysexecutive syndrome may seem nearly impossible (Alderman, 1991). Not only because EF are involved in so many aspects of functioning in daily life, but mainly because the core feature of the dysexecutive syndrome is an inability to change and adapt behaviour. This does not mean that it really is impossible to treat these problems, but it requires taking into account those factors that make EF such complex and essential functions. Only then an intervention can be designed that is clinically relevant: improving executive functioning in daily life. The first factor is related to the fact that the term 'executive functioning' actually includes many different functions. It follows that the dysexecutive syndrome can differ in individual patients, whereby the diverse elements of EF can be differentially impaired. For a treatment to be clinically relevant it should be multifaceted (aimed at improvement of the full range of EF) and offer the possibility to adjust the exact contents to an individual patient. Another important factor to take into account when designing a treatment concerns the level of functioning on which treatment is effective. Preferably, interventions for the dysexecutive syndrome should be aimed at improving executive functioning in daily life. To succeed in that, treatment should involve contextually rich activities as abstract training of strategies, outside a realistic real life

context, does not generalize to real life situations (Brouwer, van Zomeren, Berg, Bouma, & de Haan, 2002). Furthermore, to ensure that patients are able to apply the strategies they learned during treatment, transfer should be an integral element of the treatment. A prerequisite for learning strategies and applying them in daily life is that patients must be aware of their problems and be motivated to complete a treatment. In addition, the ability to self-initiate behaviour facilitates transfer from the learning situation to other activities. However, impairments in self-awareness and self-initiation are frequent executive functioning deficits following brain injury (Fischer, Gauggel, & Trexler, 2004; Hart, Sherer, Whyte, Polansky, & Novack, 2004; Marin, 1997; Prigatano, 1991). Therefore, there should be a focus on these impairments in any neuropsychological rehabilitation treatment of the dysexecutive syndrome.

Plasticity

Regarding plasticity, the 'Kennard principle' (Kennard, 1936) has long been the leading opinion. This principle is based on the child's brain and holds that impairments due to brain injury at younger age show better recovery than when injury is suffered at older age. Hebb (1949) questioned the principle based on his research on children who had suffered frontal lesions and in most cases showed the opposite pattern. He speculated that the development of frontal functioning directly depends on the state underlying brain areas are in at critical moments in development. These ideas have been supported by research. For instance, in studies on the effects of early brain injury, frontal lesions have shown to result in 'emerging deficits': problems only became apparent at a certain critical moment in their development, when these children were expected to develop executive functioning and did not (Eslinger, Biddle, & Grattan, 1997; Eslinger, Biddle, Pennington, & Page, 1999; Eslinger, Grattan, Damasio, & Damasio, 1992; Tranel & Eslinger, 2000). In relation to plasticity, Hebb further suggested, and research supported this, that synchronous firing of pre- and post-synaptic cells leads to new synaptic connections: "cells that fire together, wire together". When two neurons or groups of neurons become disconnected due to a lesion, their simultaneous activation within the network they are part of can result in reconnection. Connectionist models come in two main forms: those in which connections between neurons are dependent on input, and those in which connections strengths are specified. For rehabilitation, the main implications of these models are that rehabilitation should be intense, and nearly error free, but must allow enough errors or be sufficiently challenging to increase new connections. However, these two approaches are too limited to capture human learning. Extra, for a theory on human rehabilitation essential, information is provided by biological theories. These theories, Hillis (2005) states, describe that

the brain has more localisation of function than is required according to connectionist models, and that this localisation is modifiable, either by lesions, change of input, or by experience: intense practice or rehabilitation. Another biological view on rehabilitation is that change in connection strength in the brain depends on chemical milieu. Different neurotransmitters, for example, have been proven to play a role in the experience of reward, punishment, or emotional state. Wilson (1997) observed that feelings, emotional state, and social and behavioural consequences have important influences on rehabilitation. The influence of these neurotransmitters on synaptic plasticity may explain why.

Before further focussing on the mechanisms underlying recovery in the damaged brain we have to consider how a healthy brain changes in response to experience. Kelly and Garavan (2005) describe three patterns of practice-related activation change: increase, decrease or functional reorganisation of activation in those areas involved in task performance. Reorganisation can be further subdivided in two types: *redistribution*, in which the functional anatomy remains basically the same, but the contribution of specific areas to task performance changes as a result of practice. The other is: *'true' reorganisation*, which shows an actual change in the location of activation. This means that neurobiologically and cognitively different tasks are being performed before and after practice. There are several factors influencing which pattern is most prominent and they provide information on the mechanisms likely to underlie the changes in activation. The first is the effect practice has at a cognitive level. If practice results in a shift to another cognitive process underlying task performance, a *'true' reorganisation* of activation will be observed. This is for instance the case in mirror reading which, early in learning, requires visuospatial information processing and after some practice, as performance becomes automatic, changes in object recognition (Poldrack, Desmond, Glover, & Gabrieli, 1998). *Redistribution* after practice, depends on the increased role of task or process specific areas and a decrease of the influence of control and attentional areas, mostly in the prefrontal cortex (Kelly & Garavan, 2005). A second factor influencing the practice-related activation change is task domain. While practicing a sensory or motor task results in an increase of activation, training of cognitive tasks results in a decrease of activation in the task specific areas. This has for instance been found in subjects practicing a working memory task (Jansma, Ramsey, Slagter, & Kahn, 2001) and after a training of alertness (Sturm et al., 2004). Other factors, partly overlapping with the first two, include: the point in practice at which participants are imaged, pre-existing individual differences, and task difficulty.

Similar to changes in healthy brains, experience-dependent neural processes after brain injury have been described to take several forms. These plastic changes have been reported after the period of spontaneous recovery and they show similarities with practice- and experience dependent changes in the healthy brain (Mateer & Kerns, 2000). Grady and Kapur (1999) propose the following types of changes: reorganisation within an existing neuronal network; recruitment of new areas or use of an alternate network; and inclusion of regions surrounding the lesion. Research has shown there are several factors influencing plasticity. More knowledge on these factors is essential to stimulate functional recovery and develop effective rehabilitation methods. Robertson and Murre (1999) considered the role of Hebbian learning (Hebb, 1949) in recovery after brain injury and concluded that stimulation should only be used when there is an intermediate loss of connections. Mild brain injury would show spontaneous recovery through self-repairing processes (the Hebb effect) and severe lesions with damage to large neuronal networks would show no recovery at all. In the intermediate lesions, the damaged connections between neurons could be restored by 'guided recovery': external stimulation causing simultaneous activation of disconnected areas which would then lead to recovery of damaged connections on the basis of Hebbian learning. Each patient should therefore be assessed whether she or he could benefit from stimulation and what form of stimulation exactly would lead to the best results. Robertson (2005b) states that 'guided recovery' is best applied in recovery of a function showing some residual capacity. This capacity can remain unnoticed due to low level arousal, poor awareness of deficit, inhibition by competitor circuits, or inadequate ability to pay attention to relevant behaviours. The influence of these factors should be reduced as much as possible in order to optimise the circumstances for recovery through plasticity. There are different types of stimulation: general stimulation (or environmental enrichment), or specific stimulation. This last type can further be subdivided in bottom-up and top-down specific stimulation. In both, attentional processes play a large role: the first involving external help to focus attention on a certain action, the second demanding a person to consciously pay attention when performing an action. Linking the concept of Hebbian learning to these types of stimulation, the conclusion would be to offer specific stimulation only. Moreover, because some plastic changes have shown no relation with functional recovery or even have a negative influence on recovery (Beauvois, 1982; Naeser et al., 2005; Pizzamiglio, Galati, & Committeri, 2001). Despite all the research on stimulation of plasticity, there still is a lot unknown. Perhaps plasticity can be influenced directly through pharmacotherapy, or ways can be found to influence genetic factors, which are known to play a role in recovery after brain

injury (Jordan, 2007). Additionally, the timing of rehabilitation may be critical (Robertson, 2005b).

Evaluation of recovery from the dysexecutive syndrome

The influence of neuropsychological rehabilitation on recovery of functioning after brain injury is studied at different levels to gain more insight in, for instance, therapy effectiveness or recovery prognosis of a specific patient on the function being trained. Robertson (2005b) stresses the importance of research on this topic: "rehabilitation can harm as well as help" (p. 281). According to him it is important to know what the exact underlying mechanisms are that make neuropsychological rehabilitation work. Otherwise therapists risk wasting precious time on ineffective treatments, damaging patients through harmful treatment and allowing atrophy of the brain by failing to give correct stimulation. In general, prospective randomized controlled trials evaluating treatment of the dysexecutive syndrome are sparse (Cicerone et al., 2005; Cicerone et al., 2000). Some well designed studies have been carried out addressing one or more aspects of executive functioning, like problem solving (Cramon von & Matthes-Von Cramon, 1994; Foxx, Martella, & Marchand-Martella, 1989), goal management (Levine et al., 2000) or self-regulation (Medd & Tate, 2000). Until now, very few multifaceted treatment protocols are described of which the effects were evaluated according to basic methodological criteria. A protocol that was developed according to these standards and aimed at the full range of EF has proven to be very successful (Spikman, Boelen, Lamberts, Brouwer, & Fasotti, 2009). In search of the effective processes in neuropsychological rehabilitation all possible instruments should be used in order to refine and improve treatments (Robertson, 2005a). Furthermore, in order to be certain a treatment is effective, it is essential to show changes not only in people's lives, but in their performance and their brains (O'Connor, Manly, Robertson, Hevenor, & Levine, 2004; Sturm et al., 2004). Functional neuroimaging is a potentially powerful tool in this scientific verification of neuropsychological rehabilitation (Pizzamiglio et al., 2001; Ricker, Hillary, & DeLuca, 2001) and it offers the opportunity to study the link between neuropsychological rehabilitation and plasticity.

There are relatively few neuroimaging studies on the rehabilitation of executive functioning after brain-injury. The studies that have been conducted have very diverse research designs: dealing with spontaneous recovery or recovery after therapy and using resting state or activation paradigms. Many studies addressing the rehabilitation of executive functioning have been done in patients with schizophrenia. These patients can show symptoms of the

dysexecutive syndrome. The negative syndrome, a sub-syndrome of schizophrenia, is associated with slowing of mental processing and deficits in tasks that require planning abilities (Semkovska, Bedard, & Stip, 2001). Wykes (1998) states that the ability of patients with schizophrenia to utilize social and occupational skills is a direct consequence of their executive dysfunctions in combination with memory and attention deficits. Therefore, although not a type of acquired brain injury, a few studies with patients suffering schizophrenia will also be discussed.

Resting state studies measuring recovery after cognitive rehabilitation aimed at EF, showed an increase of prefrontal blood flow after training of patients with acquired brain injury. These changes were linked to neuropsychological test results and a more active daily life (Laatsch, Jobe, Sychra, Lin, & Blend, 1997; Laatsch, Pavel, Jobe, Lin, & Quintana, 1999). Activation studies on neuropsychological and cognitive rehabilitation in patients with schizophrenia led to a similar observation of increased frontal activation (Penades & Mateos, 2002; Wykes et al., 2002). In Wykes' study, three groups were compared: patients receiving treatment focused on EF, patients receiving a control treatment, and a healthy control group. At baseline, patients showed less frontal activation than healthy controls during a working memory test. After treatment the two patient groups showed an increase, while the healthy controls showed a decrease of activation during their second scan. Moreover, marked increases in brain activation in regions associated with working memory were found in those patients who benefited most from cognitive rehabilitation. These differences between patients and healthy controls were also found in a functional neuroimaging study by Sturm et al. (2004) on a training of alertness in stroke patients. These results indicate that, contrary to what is found in healthy controls, frontal activation increases in patients after training of a cognitive task, both in activation and in resting state studies. In contrast, a number of functional neuroimaging studies comparing activation at baseline of patients who suffered traumatic brain injury with healthy controls have demonstrated that frontal activation in patients was in fact more intense or wide spread during the performance of cognitive or executive functions tests (Christodoulou et al., 2001; McAllister et al., 1999; McAllister et al., 2001; Ricker et al., 2001; Scheibel et al., 2003). As was also discussed earlier, a possible explanation for this is that patients need to recruit more brain areas and use those areas more intensively during the performance of a certain task. As well as activation changes within an existing network there is also proof of recruitment of new brain areas after brain injury. In a study using repetitive transcranial magnetic stimulation (rTMS), a temporary impairment in the prefrontal areas associated with working memory was inflicted on the subjects. Other areas were then found activated during the performance of a verbal working

memory test. Which areas took over depended on the location of the rTMS (Mottaghy et al., 2003).

Not only can functional neuroimaging provide information on the link between neuropsychological rehabilitation and plasticity, it can also be a valuable addition to behavioural studies. Intact performance after brain injury does not always imply normal neuronal responses. Functional neuroimaging has shown that alternative neuronal and cognitive mechanisms may support the task and mediate recovery (Price, 2002). Alternative neuronal routes or increased activation in patients can for instance offer an explanation as to why they report a task to be more effortful (Cramer, 1997; McAllister et al., 1999; Perani et al., 2003) . Furthermore, knowledge of the underlying processes and of the brain regions critical to recovery of functioning, can aid in designing a treatment (Strangman et al., 2005), the decision which treatment to give (Munoz-Cespedes et al., 2005), at which point in the rehabilitation process to start with treatment, and whether or not to give treatment at all in the case of a specific patient (Ricker et al., 2001; Robertson, 2005b). Finally, hard scientific evidence on neuropsychological rehabilitation methods is essential in the pursuit of acceptance and respect for these methods and funding for research on the subject (Robertson, 2005a). Bigler (2003) adds that neuropsychology should keep up with advances like neuroimaging and incorporate them into their practice, as "neuropsychology is the field that connects neural function to behaviour" (p.615). Concluding, further research in this field is strongly recommended, but to ensure that the energy and funding spent will have been worthwhile there should be a strong emphasis on clinical relevance.

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