Chapter 6
General Discussion and Conclusions

The aim of this thesis was to perform an ecologically valid evaluation of a newly developed multi-faceted treatment protocol for the dysexecutive syndrome in patients with brain injury (Spikman et al., 2009). The methods available for this were: functional Magnetic Resonance Imaging (fMRI), neuropsychological tests and questionnaires.

Within the several sections of this thesis, executive functions (EF) proved to be complicated functions to perform research on, especially as the research was aimed to have clinical relevance. There were several factors responsible for this. To start with, EF are hard to capture in traditional neuropsychological assessment. They are the functions that enable a person to initiate, regulate, and introspect upon behaviour over a long period of time without external cueing. A situation in which this is brought into practice is best described as 'multitasking' (Burgess et al., 2005a). The authors distinguish this from multiple-task performance by stating that multitasking involves an ill-structured situation and the activation of delayed intentions. Many factors inherent in an assessment situation make it quite different from daily life situations that require executive functioning: cues (Spikman et al., 2000a), absence of distraction, structure provided (Chamberlain, 2003), and the abstract and artificial tests itself. Furthermore, EF tests make demands on other (non-executive) cognitive functions (Rabbitt, 1997). Finally, most tests only assess one or two of the elements essential for executive functioning and ignore the remaining elements, particularly motivation and emotion. This can result in brain injured patients performing on the level of healthy controls in an assessment procedure while experiencing severe dysexecutive problems in daily life (e.g. Wood et al., 2004). Moreover, results on neuropsychological tests are not easily translated to a person's level of executive functioning in daily life. This "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" (Sbordone, 1996 p.16) is termed: ecological validity. In functional neuroimaging research it is even more complicated, and there probably has been less urge, to design ecologically valid tests. Movement restrictions, elementary research questions without a clinical context, or, in patient research, restrictions caused by physical or cognitive impairments of the participants, have resulted in a large range of tests with too much structure provided by the test and therefore hardly any element of executive functioning left.

Besides assessment, neuropsychological rehabilitation of the dysexecutive syndrome is extremely challenging. One of the reasons for this lies again in the fact that many elements

together constitute executive functioning. It follows that the diverse elements can be differentially impaired in individual patients. The main challenge, however, in treating the dysexecutive syndrome is that it involves impairments in self-awareness and an inability to change and adapt behaviour (Fischer et al., 2004; Hart et al., 2004; Marin, 1997; Prigatano, 1991). Only when taking these challenges into account, an intervention can be designed that is clinically relevant: improving executive functioning in daily life. Some well-designed studies have been carried out addressing one or more elements of executive functioning, but very few multi-faceted treatment protocols are described. The protocol that we had the opportunity to evaluate was aimed at the full range of EF and did provide the possibility to tailor it to the patients' exact dysfunctions.

These challenges in designing ecologically valid EF tests and clinically relevant treatments for the dysexecutive syndrome are all the more important to take into account because EF are essential for independent functioning. What is more, EF are indispensable in the process of resuming previous activities after brain injury. To guide a patient best in that process, therapists need tests with ecological validity and a treatment that provides patients with those strategies relevant to their specific impairments and their daily life activities. Concluding, in research on EF the relevance of the results for daily life situations should be the focus of attention. This might complicate the research design, but ensures results to have a large impact on patients' lives.

Summary of results

A new EF test for fMRI was developed: the Daily Life Planning Test (DLP). It involved subgoaling of everyday activities, resembling the context and content of the treatment protocol. Brain activation patterns were analysed in 19 healthy subjects performing the DLP and the fMRI version of the Tower of London (ToL; Shallice, 1982); a test used very often in fMRI research on EF. As expected, results showed mainly similarities in brain activation between both tests. The DLP is a valuable addition to the ToL in EF research because it involves other aspects of the planning process. Aspects that probably play a role during planning in daily life.

Parallel to the development and evaluation of the new test for fMRI, a new office based EF test was evaluated: the Executive Secretarial Task (EST; Spikman et al., 2007). 92 participants were assessed: 35 brain-injured patients and 57 controls. Analyses showed the EST to be sensitive to executive problems, and to have concurrent and ecological validity.

In research on the multi-faceted treatment protocol, 75 outpatients with acquired brain injury and a dysexecutive syndrome were treated either with that protocol (experimental

treatment) or with a computerized cognitive training package aimed at improving general cognitive functioning (control treatment). Satisfaction and subjective well-being were on the same level in both treatment groups. However, the experimental group did perform better on a composite measure and this effect lasted at least until six months after treatment. In this composite measure three domains of daily life were combined: the ability to set and accomplish realistic goals; the ability to plan, organise and regulate a series of real life tasks (EST); and the ability to resume previous roles with respect to work, social relations, leisure activities and mobility.

Finally, six stroke patients who were assigned to the experimental treatment group also participated in the fMRI study. They were scanned while performing EF tests before treatment, after treatment and at follow-up. Additionally, anatomic scans, neuropsychological tests, and questionnaires were administered. At all three measuring points the patients showed less frontal activation than the healthy controls for which they compensated through extra parietal activation. Over time, frontal activation increased in those patients who became more active in daily life. The results of this study led to suggestions to improve neuropsychological rehabilitation.

Ecological validity in executive functioning research: implications

Neuropsychological tests and rehabilitation

This research project led to suggestions for interesting further research as well as suggestions to improve clinical practice or research on executive functioning in the future. The first remark concerns the use of traditional neuropsychological tests for EF. In clinical practice as well as in research, neuropsychological tests are still used that have weak psychometric properties and lack ecologically validity. This is partly the reason why in most cases there is no translation provided from test results to daily life. In clinical practice this leads to uncertainty in patients and their proxies on what a certain test score may mean for everyday functioning, how they should adapt to the new situation after brain injury and what might be the most likely problems they will encounter. In research it leads to studies with no actual meaning for clinical practice. In both fields other measures should be considered and the presentation of test results, either when informing the patient about his achievement or colleagues about research results, should be critically reflected on. In our study the EST proved to have good psychometric properties and ecological validity. However, also in this case neuropsychologists should be

aware that test scores are presented meaningfully: translated to daily life other than simply reporting scores to be either high or low.

Besides being critical about the use of traditional assessment tools, neuropsychologists might perhaps also be stimulated to use alternative measures more often. In the evaluation of the treatment protocol such an outcome measure was included: the ability to set and accomplish realistic goals. After half of the sessions, patients were asked to formulate goals they wanted to achieve through the treatment. After treatment patients indicated whether they had reached their goals and to what extent. This measure proved to be useful in more than one way. Not only did it provide a guideline for the main issues to be dealt with during the treatment, but also did it provide a very natural outcome measure and motivate patients and their proxies to complete the treatment. A comparable method was studied and advocated by Wilson, Evans and Keohane (2002). With the addition of goal planning to neuropsychological rehabilitation the use of standard neuropsychological tests can be restricted to determining the level of cognitive and executive functioning of a patient before treatment instead of determining treatment success. A kind of goal planning is probably already being used by many clinical neuropsychologists, but applying it in the standardized manner as we did will add to its value. At the other side of the spectrum, in research, comparable measures could aid translation of research results to clinical practice.

In summary, the larger problem seems to be: too little research in clinical practice and too little clinical practice in research. Whenever both fields are combined, results prove that they are valuable additions to each other. The successful test and treatment design in our study demonstrated this. The EST showed that it is possible to design a test of which the results can easily be translated to a patient's daily life. The treatment protocol allowed flexibility from the therapists. We are certain that this greatly added to the high ratings the protocol received from both therapists and patients and to the fact that there were very few patients who dropped out. Both the EST and the treatment protocol were developed in a research context and fulfilled a need of clinical practice. Hopefully, there will always remain neuropsychologists making the effort of combining research and clinical practice, but creating possibilities so more can do the same would benefit the whole field of neuropsychology.

Functional neuroimaging in neuropsychology

Within this neuropsychological context, the possibilities of functional neuroimaging were further explored and pondered on. Results of our and other studies show that, at present, the additional value of functional neuroimaging to the traditional neuropsychological research

methods mainly lies in offering suggestions for new hypotheses: giving neuropsychologists the opportunity to look beyond well-known territory. However, standard application of the method in neuropsychological research is not yet likely or desirable. It is still a very expensive and time consuming technique, there are often only limited facilities available, and it requires a high degree of expertise. These external factors often significantly restrict researchers in their study design. For instance, in our fMRI study the costs and limited time and scanning facilities were the main reasons why the healthy control group was scanned only once in contrast to the patients who had three scanning sessions. An inclusion of multiple scanning sessions for the healthy control group would have improved the study. As there is the effect of possible changes in brain activation patterns due to repeated measurements to take into account. Clearly, this addition would have made the comparison between brain activation of healthy controls and that of the patients, who had multiple scanning sessions, more accurate. Along the same lines, another limitation of our fMRI study was that only three patients were presented with the DLP. This was mainly due to the developmental process and the testing phase of the DLP costing more time than expected. Results of the DLP in the patients and healthy controls suggested it could offer valuable extra information. Therefore further research should be done in which the DLP is presented to larger groups of brain injured patients, including a variety of aetiologies, and with or without a dysexecutive syndrome. Another group of restrictions are those linked to the actual method of functional neuroimaging and have for instance led many researchers to include tests that are abstract and artificial representations of reality. This issue has been extensively discussed elsewhere in this thesis and motivated us to develop the DLP.

Besides its application in research, the actual use of functional neuroimaging in neuropsychological clinical practice still seems a long way to go to. This is also a larger step to take as clinical practice presents research with its own, additional restrictions: the wide variability in anatomical and functional organisation after brain injury, patients' difficulty to comply with movement restrictions, extra time needed relative to healthy volunteers, and test compliance. We encountered even more restricting factors in our study. Finding patients willing to undergo three scanning sessions was not as hard as we expected, but it was difficult to find patients meeting the most essential term of fMRI research: no metal implants. Furthermore, the scanning sessions proved to be more tiring than expected. Not only because scanning itself took almost two hours, but also because the journey to and from the neuroimaging centre was tiring and because for some patients the scanning sessions brought back traumatic memories to the period just after their brain injury. Due to all these factors we could only include six patients in our fMRI study. Besides that being a fairly small group, these patients were all elderly men who

had suffered stroke and were included in the experimental treatment group. In a small group like this the more similarities the better as a homogeneous group allows for comparison between participants. It would have been interesting though to compare the data in the present study with data of patients assigned to the control treatment, patients with other aetiologies, younger patients, or female patients. The fact that in the present study, one patient stopped treatment on his own initiative, but was still willing to undergo the scanning sessions did provide us with a sort of control condition. However, as it was his own choice to stop, he could not be considered as a methodically correct control patient. Moreover, a large limitation to take into account when performing comparative or group analyses in functional neuroimaging is that there are many unknown influences of the differences in brain injury on data analysis.

Concluding, functional neuroimaging is a method that confronts researchers with many additional restrictions or considerations besides, for instance, ecological validity. It would be unfortunate, however, if ecological validity would just be seen as another complicating factor to take into account in a research design, perhaps even leading to the decision to ignore it. Making a research design (more) ecologically valid does require extra effort and time, but only then neuroimaging can be a valuable instrument which is worth the funding and research time spent. A first suggestion to improve ecological validity of functional neuroimaging research in neuropsychology is to make sure that the test designed for the scanner really measures what it is supposed to. A method to do this is comparing the fMRI-test, in an office-based version, with existing neuropsychological tests prior to the actual use inside the scanner. In this way clarifying if and to what extent it depends on other (cognitive) abilities like visuospatial processing, memory, or attention. This provides the opportunity to refine the test before starting the scanning sessions. Of course it is impossible to filter out all other cognitive or executive functions and develop a "pure" test of one function. Therefore, to control for the influence of those other abilities it would be wise to assess each participant on a battery of neuropsychological tests besides placing them in the scanner. Additionally, as many factors secondary to the scanning itself as possible should be taken into account. For instance: time of the day; quality of sleep; nervousness; and intake of substances as caffeine, nicotine, or drugs. These should be registered and kept constant, or added as a factor to data analyses besides the usual factors as age, sex, and education. All these factors can be of influence on a person's achievement, brain activation, or test compliance. Finally, behavioural data during the neuroimaging session should be collected: reaction time, answers per item, and maybe even measures like heart rate or eye movements. These can be used, again, as factors controlling that a participant has really been doing what he was supposed to do and that all participants (or one

participant across multiple scanning sessions) have been doing the same. It makes comparisons within and between participants more accurate.

Even if all the advises above would be taken into account, the question still remains whether specifically executive functioning can be captured in a test, let alone a test inside a scanner. As that is a very structured environment, full of cues, only allowing a short time span, not allowing multitasking, and where motivational or emotional elements are impossible to include or control. Tests in that environment are as abstract and artificial as they can be. Should we then keep on trying to capture EF in functional neuroimaging research? The answer undoubtedly should be: yes. The importance of research on these functions is quite obvious and has been extensively discussed in this thesis. Besides that, developments in office based testing have proven that it is possible to develop ecologically valid tests of EF. In functional neuroimaging it will take more time and a lot of effort, but in the end this could become a valuable research instrument for neuropsychologists. For this to really happen, it is essential that researchers do not confine themselves to the scanning room, but (dare to) include clinical practice in their frame of reference.