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Doin’ it right
Assessment and errorless learning of executive skills after brain injury

Dirk Bertens
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Proefschrift

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te Roosendaal
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One  General introduction
The first person to receive the treatment that I present in this thesis was Mr. S (67 years old). Two years prior to the treatment, Mr. S had had a stroke, after which he reportedly saw a steep decline in his ability to manage and complete typical daily activities. For example, Mr. S reported that his previously well-maintained and organized garage had become chaotic, yet he felt he had no idea as to how this had happened, or how reorganize the space. He also seemed unable to maintain simple, everyday goals in mind; he twice flooded the kitchen by forgetting he was washing the dishes and leaving the faucet running to ‘briefly’ go into the garden to dispose of garbage. Like many patients with acquired brain-injury (e.g., due to stroke or traumatic brain injury) Mr. S experienced executive function problems which had a considerable impact on his daily life.

This case example highlights the importance of executive dysfunction, and emphasizes its effects on everyday life. In this theses, I will first elaborate on the theoretical foundations of executive function. Next, I will focus on the assessment of executive function and the use of ecologically valid methods, that is, neuropsychological testing that approximates everyday executive function. Subsequently, I will describe several training methods that are (or may be) used for training everyday tasks in executively impaired brain-injured patients. Finally, I will give an outline of the studies covered in the chapters of this thesis.

**Executive function**

Executive functions are typically described as a set of higher level cognitive abilities that control and regulate other abilities, including the initiation and regulation of goal-directed behaviour in complex and unstructured situations (Alvarez & Emory, 2006; Elliott, 2003; Norman & Shallice, 1986; Stuss & Alexander, 2007). Executive function is often referred to as an umbrella term for various complex cognitive processes and sub-processes needed to achieve a particular goal (Barkley, 2001; Lezak, Howieson, Bigler, & Tranel, 2012). Subsequently, attempts to define executive function often resort to the proposal of a list of subcomponents (i.e., executive functions), such as planning, inhibition, reasoning, working memory and cognitive flexibility), which reflects the point that executive function might be considered as a non-unitary concept (Elliott, 2003). Packwood, Hodgetts, & Tremblay (2011) reviewed 60 of the most frequently cited studies and identified 68 different subcomponents of executive function. This profusion of subcomponents makes the concept of executive function unclear and difficult to operationalize (Andres, 2003; Jurado & Rosselli, 2007).

Ylvisaker, Szekeres, & Feeney (1998) attempted to narrow down the number of subcomponents of executive function from a clinical point-of-view. They
distinguished eight essential aspects of executive functions: **self-awareness of strengths and needs**, realistic and concrete **goal-setting**, planning the steps to these goals, **self-initiating** these plans, **self-monitoring** and evaluating performance according to plan and goal, **self-inhibiting** behaviour not leading to the goals set, **flexibility and problem solving** when situations cannot be dealt with according to plan, and finally, **strategic behaviour**, that is, transfer of successful behaviours to other situations. These aspects can be differentially impaired in brain-injured patients, leading to a heterogeneity of dysexecutive symptoms. Others have attempted to gain a more coherent structure through factor analyses (Fisk & Sharp, 2004; Huizinga, Dolan, & Van der Molen, 2006; Miyake et al., 2000). Miyake et al. (2000), for example, administered several experimental tasks and five frequently used executive function tests: the Wisconsin Card Sorting Test (WCST), Tower of Hanoi (TOH), random number generation (RNG), operation span, and dual tasking in 137 healthy participants. Confirmatory factor analysis identified three target executive functions: **shifting**, **inhibition** and **updating**. However, these three executive functions were not completely separable, but moderately correlated constructs, indicating some underlying commonality. Thus, on the one hand, the three factors indicate executive functions to be a diversified construct. On the other hand, the underlying correlations are also compatible with more traditional unitary theoretical proposals that describe common mechanisms across different executive functions. In Norman and Shallice’s model (1986; see Figure 1) for example, executive function is described as a control mechanism called the ‘Supervisory Attentional System’ (SAS). There are two main assumptions that underlie the model. The first is that the control of selecting routine actions and thought operations is decentralized, a process called ‘contention scheduling’. Thus, within routine situations the appropriate response is selected by automatically activating schemata based on contextual information. However, in new or non-routine situations such automatic responses are not available, insufficient or competing, so that a higher control and scheme selection mechanism (the second assumption), the SAS, is necessary.

An example of a non-unitary, though still parsimonious approach, is the model of Shallice and Burgess (1996). Instead of describing executive functions recurring to a multitude of subcomponents, the authors describe three general stages that one must go through when facing a new or complex situation and the concomitant **construction of temporary new schema**, implementation of temporary new schema, and **assessment and verification**. The output of the model is a behavior that emerges from these three general principles. All aforementioned executive functions or subcomponents could be considered as being examples of different outputs or behaviors deriving from these basic underlying executive functions.

**Figure 1** The Mark II Supervisory System model of Shallice & Burgess (1996).
Goal neglect and goal-directed behaviour

Regardless of their unitary or varied character, executive functions play a key role in the accomplishment of particular goals in a flexible manner (Funahashi, 2001). Two decades ago, Duncan (1986) already proposed a theory on the control of behaviour by its desired results, relating executive functions to goal-directed behaviour. This author came up with the idea that any (everyday) activity requires that a list of goals is devised to generate a structure of action, by which those goals are achieved. In multistep activities, the reduction of the difference between current states and goal states guides action selection. A plan of action consists of a hierarchical structure of successive sub-goals that unfolds as a result of the requirements and constraints on behaviour. Duncan suggested that executive dysfunction represents a defect in the process of reducing the mismatch between current states and goal states. Thus, disorganization of behaviour is the consequence of a failure in the ability of goals to seize and maintain control over the course of actions until they have been achieved (and the end goal attained). The behaviour of executively impaired individuals may be characterized by an inability to retain a stable purpose of behaviour on the one hand, and the insertion of irrelevant actions on the other hand. Such irrelevant or ill-judges intrusions, that seems to be the result of an insufficient monitoring, and the apparent neglect of task demands is called goal-neglect (Duncan et al., 1996).

At a more behavioural level, executive function and goal-directed behaviour have been conceptualised into four different components: volition, planning, purposive action, and effective performance (Lezak et al., 2012). Volition is described as the ‘capacity for intentional behaviour’ and is crucial for the other three components. Planning is related to the organisation of the (task) steps needed to achieve a goal (i.e., an everyday task). Planning involves the ability to overlook a complex situation and its environmental constraints. It calls upon anticipatory skills and the ability to consider behavioural alternatives. Next, purposive action is important for initiating a particular plan and at the same time ignoring irrelevant or competing task steps. Continuous monitoring and bearing in mind the main goal is needed for effective performance. When required, execution should be stopped, and corrected by flexibly switching to alternative behavior. This adjustment of behavior asks for the ability to keep an end-goal and its sub goals actively in mind over longer periods of time. Errors have to be monitored, recognised and when needed, corrected. When the intended final goal has been achieved, this has to be acknowledged and execution has to be stopped in time. Patients with (dys)executive problems may stop acting before attaining the end-goal or even continue acting when this end-goal has been achieved (Lamberts, 2009).

The model of Brouwer & Schmidt (2003; see Figure 2) is another example of a multiple process model. This model is based on the Norman and Shallice model (1986). Above the horizontal dotted line psychological processes representative for executive functions such as self-monitoring, motivation and working memory are indicated. Below the dotted line implicit automatic aspects of information processing and memory are listed, that is contention scheduling. Supervisory attentional control of schema-driven information processing is activated when a discrepancy is sensed between actual state and required goal attainment. This framework complements the model of Norman and Shallice by adding the awareness of (dys)functioning (i.e., the ‘monitor’) through behaviour monitoring, which plays a critical role in activating the SAS.

The scientific literature (still) points to both unity and diversity of executive functions and indicates that both perspectives need to be taken into consideration in developing a theory of executive functions (see Duncan, Emslie, Williams, Johnson, & Freer, 1996; Miyake et al., 2000), as already suggested more than forty years ago (Teuber, 1972).

Figure 2 Revised mental schema theory of Brouwer & Schmidt (2003).
Executive dysfunction after acquired brain injury

Executive functions are typically related to the frontal regions of the brain (Luria, 1966; Shallice & Burgess, 1991). Luria (1966) proposed that the prefrontal areas of the brain are superimposed on all other cortical areas, enabling the prefrontal regions to perform a more global and supervisory function of regulation and integration of behaviour. He described that damage to the frontal lobes resulted in deficits in problem-solving, decision-making, and active thinking. These symptoms were part of the so-called ‘frontal lobe syndrome’, a disorder concerning the overall organisation of cognition and action. Later lesion and neuro-imaging studies (see for example Alvarez & Emory, 2006; Elliott, 2003) have confirmed the close relationship between executive function and the frontal lobes. However, more recent studies emphasize that not only frontal areas but a widespread network of brain regions is activated and involved in executive functions. Therefore, executive impairments are also associated with lesions in non-frontal brain areas (Alvarez & Emory, 2006; Godefroy, 2003) such as the parietal cortex, basal ganglia, thalamus, and cerebellum (Collete et al., 2005; Monchi, Petrides, Strafella, Worsley, & Doyon, 2006; Wager, Jonides, & Reading, 2004; Wager & Smith, 2003).

To circumvent the aforementioned localization problem, Baddeley (1986) introduced the concept of ‘dysexecutive syndrome’. This was a functional definition of executive deficits, rather than a classification of patients on the basis of anatomical lesion localization. The dysexecutive syndrome consists of several cognitive, emotional and behavioural symptoms. Cognitive problems may include, but are not limited to, impairments in working memory, inhibition, planning and organization, initiation, monitoring and flexibility (Alvarez & Emory, 2006; Friedman et al., 2006). Behavioural symptoms may include poor organization of stories and conversations, difficulties in keeping up with the demands of work-related and social obligations, and an increased level of distress when confronted with a changed plan. Social-emotional behaviours may include insensitivity to the feelings of others, lack of emotional profundity and lack of insight (Anderson, 2008; Morgan & Heaton, 2009). Although many of these dysexecutive symptoms regularly co-occur, it is common to encounter patients who suffer from several, but not all of these symptoms. Luria (1966) has suggested that apart from the clinical diversity, executively impaired patients were more specifically impaired in situations requiring goal formulation, planning, carrying out goal-directed plans, and verification. As a consequence, impairments in executive functioning lead to the disorganization of everyday functioning (Mateer, 1987) and even subtle executive deficits may lead to substantial difficulties in performing everyday-life tasks (Boelen, Spikman, Rietveld, & Fasotti, 2009).

In the clinical practice of cognitive rehabilitation after acquired brain injury there are two main aetiologies underlying the dysexecutive syndrome: stroke and traumatic brain injury (TBI). TBI results in brain damage (typically diffuse axonal injuries) due to an external physical force (with or without skull fracture). In the more severe cases it is accompanied by more localized damage, often affecting the frontal lobes, as well as temporal and parietal regions. A large part of the people having TBI experience executive function problems (Cicerone, Levin, Malec, Stuss, & Whyte, 2006; Ylvisaker & Feeney, 1996). A stroke is classically characterized as a neurological disorder attributed to an acute injury of the brain by a vascular cause. There are two main types: ischemic stroke due to lack of blood flow and hemorrhagic stroke due to bleeding. Executive deficits are also common in stroke patients (Poulin, Korner-Bitensky, Dawson, & Bherer, 2012; Zinn, Bosworth, Hoenig, & Swartzwelder, 2007). Zinn et al. (2007) administered a neuropsychological assessment in 47 stroke patients and approximately fifty percent scored in the impaired range on most executive function tests. Executive problems due to acquired brain injury (e.g., stroke, TBI) are persistent and may still be present many years post-injury (Boelen et al., 2009; Fonsford, Draper, & Schönberger, 2008; Spikman, Deelman, & Van Zomeren, 2000).

Assessment of executive dysfunction

Everyday executive behaviour may be assessed using self-report questionnaires such as the Dysexecutive questionnaire (DEX; Wilson, Alderman, Burgess, Emstie, & Evans, 1996) or the Executive Function Index (EFI; Spinella, 2005). However, self-report questionnaires are often not valid due to poor awareness of deficits and dysexecutive behaviour which is common in brain-injured persons with executive impairments (Bogod, Mateer, & MacDonald, 2003). Therefore, some questionnaires, such as the DEX have versions that have to be filled in by proxies as well. An alternative is the use of observation scales, such as the Executive Observation Scale (EOS; Pollens, McBratnie, & Burton, 1988), which are rated by therapists or proxies. Although these are subjective measurements, questionnaires and observation scales yield valuable information regarding everyday executive behavior and are essential to clinical assessment.

The most objective way to assess executive (dys)function is to administer neuropsychological tests. When taking into account the multifarious character of the dysexecutive syndrome these tests should measure different executive skills. Planning, for example can be assessed with the Tower of London test (Shallice, 1982). Response inhibition can be assessed with the Stroop Colour-Word Test (Golden, 1978; Stroop, 1933) or a Go/No-go test. The Wisconsin Card Sorting Test (WCST; Heaton, 1981) or the Brixton Spatial Anticipation Test (Burgess &
Rehabilitation of executive dysfunction

Goal Management Training

Based on Duncan’s theory of goal neglect (1986), Robertson developed Goal Management Training (1996), a rehabilitation technique aimed at helping patients with executive impairments to better structure (instrumental) activities of daily living (iADL). Patients are trained to “stop and think” about problems and goals before and during task execution. Goal Management Training entails learning and applying an algorithm (see Figure 4). This algorithm consists of five stages which relate to different aspects of goal-directed behavior. During stage 1, a ‘stopping moment’ is introduced to increase awareness and attention and to prepare for action. In stage 2, a goal (i.e., everyday activity) is selected. The task steps leading to this goal are defined and imprinted in working memory during stages 3 and 4 respectively. In stage 5, the steps are not only executed, but also ‘checked’ after execution. The purpose of these checkpoints is to monitor whether the actions are still in line with the plans (i.e., to ensure that behavioural output matches intentions) and to verify whether attention is still focused on the

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goal management (Grant, Ponsford, & Bennett, 2012). These selected tasks may not be functionally relevant for all participants. More importantly, by only training one or two tasks, it remains unclear if Goal Management Training contributes to better performance in a broad range of everyday activities. The aforementioned review argued that the effectiveness of Goal Management Training was superior when it was combined with other intervention methods (e.g., problem solving therapy).

Errorless learning

In addition to Goal Management Training, another well-investigated method for training everyday tasks is errorless learning. Here, the occurrence of errors during the learning process is prevented in contrast to ‘normal’ trial and error learning, in which errors may occur naturally (Baddeley, 1992). In clinical practice, several errorless learning techniques can be applied during training of complex daily tasks. Task steps can be taught using (feed-forward) verbal instructions, cue cards and visual demonstration or modeling by the trainer (De Werd, Boelen, Olde Rikkert, & Kessels, 2013). Previous studies have shown that an errorless learning approach improves task performance in patients with memory impairments (e.g., patients with Alzheimer’s dementia) compared to trial and error learning (see Clare & Jones, 2008; Kessels & De Haan, 2003).

Clinical studies investigating errorless learning have employed various theoretical frameworks to explain their findings. One account is that the beneficial effects of errorless learning in amnesic individuals reflect a failing explicit memory system, whereas implicit memory is still intact (Baddeley & Wilson, 1994; Evans et al., 2000). This theory postulates that errors made during learning are not corrected, resulting in the implicit consolidation of incorrect memory traces. Hence, preventing the occurrence of errors during learning might enhance memory performance in that only accurate responses are implicitly consolidated. Graf and Schacter (1985) however, argued that any learning observed in amnesia is only possible via the use of residual explicit memory. Therefore, others hypothesize that the beneficial effects of errorless learning operate through residual explicit memory processes and not through implicit memory processes (Hunkin, Squires, Parkin, & Tidy, 1998; Tailby & Haslam, 2003).

A more recent view predicts that the mechanism underlying the positive effects of errorless learning may heavily rely on executive function. Executive dysfunction is strongly associated with the inability to detect and monitor errors and to adjust behavior on the basis of feedback (Clare & Jones, 2008). Monitoring and correcting errors (i.e., error monitoring) during task execution increases demands on this already vulnerable executive system. Therefore, errors might
not be corrected and consequently erroneously stored into memory. During later task performance, these previously stored incorrect responses may be retrieved and interfere with the correct responses. Hence, errorless learning may optimize performance by preventing incorrect memory traces due to failures in recognizing errors. Previous studies confirmed that error-monitoring problems are present in patients with executive impairments (Bettcher, Giovannetti, Macmullen, & Libon, 2008; Yochim, Baldo, Kane, & Delis, 2009). However, very few research has been performed investigating the benefits of errorless learning in persons with executive deficits (Clare & Jones, 2008). A small number of case studies in executively impaired patients found beneficial effects of errorless learning on the learning complex semantic information (Pitel et al., 2006) and daily activities (Cohen, Ylvisaker, Hamilton, Kemp, & Claiman, 2010). These limited findings stress the need to further investigate errorless learning in executively impaired patients.

**Thesis outline**

This thesis is divided into two sections. The first section consists of two chapters and is aimed at further improvement of executive impairments. It does so, by investigating an adapted version of an existing executive function test, the Modified Six Elements Test (MSET). Part two encompasses four chapters and describes the investigation of a combination of errorless learning and Goal Management Training in the teaching of everyday tasks to executively impaired patients with brain injury.

The first chapter of part one (chapter two) describes a study in which an adapted version of the MSET was developed and administered to healthy participants. Two parallel forms were designed to prevent task-specific learning effects, allowing the assessment of executive function over the course of time. Moreover, to prevent the occurrence of ceiling effects, an adapted scoring method was proposed, taking the distribution of time spent on the six subtasks of the MSET into account. A more homogeneous distribution of time between the subtasks indicates better planning abilities.

In chapter three one of the parallel forms of the adapted MSET was administered in patients with acquired brain injury. The group was divided into patients with and without executive impairments based on several other executive tests. The aim was to investigate whether the adapted scoring method was more appropriate for discriminating between brain-injured patients with and without executive deficits compared to the conventional scoring method.

Part two starts with chapter four, which is a description of the rationale and study protocol of a randomized controlled trial (RCT) in which errorless learning and Goal Management Training were combined. This chapter describes why and how these two rehabilitation techniques were coupled when teaching everyday tasks to brain-injured patients with executive deficits, as well as the method for investigating their combined efficacy.

Chapter five is devoted to the main results of the RCT. Here, we investigated whether errorless Goal Management Training is superior for training individually selected complex daily tasks compared to conventional Goal Management Training. In addition, goal attainment as experienced by the participants and the trainers was evaluated.

Although the RCT aimed at the improvement of individually selected specific everyday tasks, in chapter six, we also studied whether the errorless Goal Management Training showed transfer to untrained executive tests. Moreover, it was examined if the experimental training contributed to a decrease in subjective cognitive complaints and an improved quality of life.

Chapter seven describes the examination of predictors of treatment success. That is, we examined for whom or under which conditions errorless or conventional Goal Management Training works (i.e., moderators of treatment outcome) and through which mechanisms these beneficial effects are achieved (i.e., mediators of treatment outcome).

Finally, in chapter eight, a general discussion of the preceding chapters is presented. The results of the studies described in this thesis are summarized and what has been learned from these studies is emphasized, highlighting the clinical relevance of these conclusions. Furthermore, several issues that remain open to discussion are described and the possible implications of these issues for future research are pointed out.
Two Reliability of an adapted version of the Modified Six Elements Test as a measure of executive function

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Abstract

The Modified Six Elements Test (MSET) is used to examine executive deficits, more specifically planning deficits. This study investigates the reliability of an adapted version of the MSET and proposes a novel scoring method. Two parallel versions of the adapted MSET were administered to 60 healthy participants in a counterbalanced order. Test-retest and parallel-form reliability were examined using intraclass correlation coefficients, Bland-Altman analyses, standard errors of measurement and smallest real differences, representing clinically relevant changes over time. For both, the test-retest and parallel form reliability, intraclass correlations were adequate and no systematic differences between the test occasions were present. Variability between the test scores was high and the test was capable of detecting real clinical changes. We show that both parallel versions of the test are clinically equivalent and can be used to measure executive function over the course of time without task specific learning effects.

Introduction

The Modified Six Elements Test (MSET; Wilson, Alderman, Burgess, Emslie, & Evans, 1996) is a neuropsychological test used to examine executive deficits, more specifically deficits in planning ability in patients with cognitive impairments of different aetiologies, such as acquired brain injury (ABI) (R. C. Chan & Manly, 2002; Emmanouel, Kessels, Mouza, & Fasotti, 2014; Gouveia, Brucki, Malheiros, & Bueno, 2007; Manly, Hawkins, Evans, Woldt, & Robertson, 2002; Norris & Tate, 2000), mild cognitive impairment (MCI) and Alzheimer’s disease (Espinosa et al., 2009), schizophrenia (R. C. Chan, Chen, Cheung, & Cheung, 2004; Liu et al., 2011) and substance abuse (Fernandez-Serrano, Perez-Garcia, Schmidt Rio-Valle, & Verdejo-Garcia, 2010). The MSET is part of the Behavioural Assessment of the Dysexecutive Syndrome (BADS; Wilson et al., 1996), a test battery aimed at assessing executive functions in an ecologically valid way (Van Beilen, Withaar, Van Zomeren, Van den Bosch, & Bouma, 2006). The MSET consists of three open-ended tasks (simple arithmetic, written picture naming, dictation). Each task consists of two parts, part A and B. Within 10 minutes, the participant has to execute at least part of each of these six subtasks. There is one rule: it is not allowed to switch directly from a subtask of one type (part A) to the counterpart of that same type (part B). Thus, a participant would not be allowed to do picture naming part A followed directly by picture naming part B (Burgess, Alderman, Evans, Emslie, & Wilson, 1998). The MSET is a simplified version of a research version of the Six Elements Test (SET), initially developed by Shallice and Burgess (1991). Where the SET contained five rules, the MSET focuses on the main rule concerning the switching order between tasks. Moreover, for the MSET the time to work on the subtasks was reduced from 15 to 10 minutes.

Several studies have shown that the MSET is a sensitive measure for detecting executive deficits in ABI patients. Bennet, Ong and Ponsford (2005) have compared the MSET to other conventional executive neuropsychological tests, identifying the MSET as one of the most sensitive tests to assess executive dysfunction. Emmanouel et al. (2013), compared the BADS subtests and demonstrated that the MSET was the best predictor to adequately distinguish anterior lesions from posterior lesions.

Although previous studies have revealed that the MSET is a valuable instrument to assess executive functioning, some limitations have been described as well. Since the MSET is susceptible to task-specific learning effects (Jelicic, Henquet, Derix, & Jolles, 2001) and no parallel versions of the test are available, the test-retest reliability of this test is poor (Wilson et al., 1996). As a result, the task is less suitable for evaluating changes over time. Furthermore, ceiling effects allow patients with mild executive impairments to perform at maximum
levels both on the raw scores or the standardized profile scores as described in the test manual. The profile scores on the test range from 0-4, and previous studies assessing ABI patients with the MSET showed a mean profile score of 3 or more (Gouveia et al., 2007; Manly et al., 2002). Therefore, mild executive deficits often go undetected with the MSET.

In the current study an adapted version of the MSET was developed and administered in healthy participants. Two parallel forms were designed to prevent task-specific learning effects, allowing the assessment of executive functioning over the course of time (e.g., clinical improvement following an intervention or spontaneous recovery). Moreover, to prevent the occurrence of ceiling effects, an adapted scoring method was proposed. That is, the conventional MSET profile score is largely based on the amount of rule breaks, which are not expected to occur in mild executive deficits. Our proposed scoring index takes the distribution of time spent on the six subtasks into account as well, as a more homogeneous distribution of time between the tasks indicates better planning abilities. In a recent study (Bertens, Frankenmolen, Boelen, Kossel & Fasotti, 2014) the validity of this adapted MSET and proposed scoring index was investigated in seventy brain-injured patients. The group was divided into patients with and without executive impairments based on six other established executive tests. Both the conventional raw scoring method and the newly proposed scoring index discriminated significantly between patients with impaired and unimpaired executive functioning. Only the proposed scoring method proved sensitive and specific within a clinically useful range, for which an acceptable cut-off score could be determined. The adapted MSET correlated significantly with four of the six executive tests.

In the present study, test-retest reliability, parallel-form reliability and ecological validity were evaluated to determine the psychometric qualities of the adapted MSET. The main aim was to investigate the reliability and equivalence of the two newly designed parallel forms of the MSET and to assess their contribution to a better assessment of executive functioning. Also, systematic differences and limits indicating relevant differences were determined to compare the equivalence of the parallel forms.

Methods

Participants

Sixty healthy participants (16 males, mean age 31.2, SD 15.0) were recruited from the network of the researchers. Inclusion criteria were age between 18 and 70 years, fluency in the Dutch language, no history of alcohol abuse, psychiatric illness or neurological disease (self-report). Educational level was determined using a 7-point scale (1: less than primary school, 7: university degree) and intellectual level was estimated using the Dutch version of the National Adult Reading Test (NART; Schmand, Lindeboom, & Harskamp, 1992). Written informed consent was obtained from all participants. Table 1 shows the demographic characteristics of the participants.

Measures

Adapted version of the Modified Six Elements Test

The adapted version of the MSET was based on the conventional MSET as used in the BADS (Wilson et al., 1996). The conventional MSET consists of three open-ended tasks, namely dictation, arithmetic and picture naming. Each task consists of two parts (A and B). Participants are instructed that they have ten minutes to execute at least a portion of all six parts, but they have to obey a switching rule: it is not allowed to switch between two parts of the same type of task. For example, it is not allowed to first complete the first section of arithmetic part A directly followed by arithmetic part B. After arithmetic participants have to switch to dictation or picture naming.

Compared to the conventional MSET, the newly developed MSET has different tasks to be carried out. Moreover the adapted MSET consists of two parallel forms to control for practice effects and to assess executive functioning over the course of time (e.g., before and after an intervention). In line with the children's version of the BADS (BADS-C; Emslie, Wilson, Burden, Nimmo-Smith & Wilson, 2003) the dictation task was replaced by a sorting task making the test more suitable for patients with language disorders (due to e.g., brain injuries, autism). Here, small objects, available in three colors, have to be sorted by color. In one version small cable lugs (part A) and tile spacers (part B) have to be sorted, in the other version small plastic wall plugs (part A) and cable ties (part B). The stimuli of the remaining tasks are presented in two booklets per task (part A and B). The two remaining conventional MSET tasks, arithmetic and picture naming, are incorporated in the adapted MSET. Arithmetic is used as one of the three tasks in version 1 and picture naming is used in version 2. Arithmetic entails calculating and writing down solutions of simple sums. The aim of picture naming is to write down the name of pictures. The third task of version 1 is pictures in categories, in which the participant has to write down the page number of a picture in the corresponding ‘category column’ in a table (e.g., a picture of a hammer belongs to the category ‘tools’). The third task of version 2 is words in categories, in which the participant has to write down the page number of a word in the corresponding ‘category column’ in a table (e.g., the word ‘trumpet’ belongs to the category ‘musical instruments’).
Executive Function Index (Dutch version)

Self-reported executive functioning in daily life was measured using the Dutch adaptation of the Executive Function Index (EFI-NL) (Janssen et al., 2009). The EFI was developed by Spinella (2005) and consists of 27 items and five subscales: Motivational drive (MD), Organization (ORG), Strategic Planning (SP), Impulse Control (IC), Empathy (EM), that cover the main aspects of subjective executive functioning. Items are recorded according to a 5-level likert scale (1 = describes me not at all, 5 = describes me very much). Higher scores indicate better executive functioning.

Procedure

The tests and questionnaire were administered by trained psychology graduate students. Both parallel forms of the adapted version of the MSET were administered with a one-to-two week interval, and the order in which the versions were administered was counterbalanced. Accordingly, for each participant two test sessions were planned. Both sessions took place in the homes of the participants, taking care that potentially distracting stimuli (mobile phone, other people, radio, television) were removed or silenced. During the first appointment (T1) written informed consents was obtained from all participants and general information (e.g., age, educational level, medical history) was recorded.

MSET scoring

For comparative purposes, we first scored the MSET in the traditional manner. Raw scores were obtained by subtracting the number of rule breaks of the number of subtasks that were performed. Subsequently, the scores were converted into profile scores using the manual of the BADS. The profile score ranges from 0 (low performance) to 4 (high performance). Next, an adapted scoring index (Bertens et al., 2014) was calculated using Equation 1, where the time spent by the participant on the longest and shortest subtask is recorded in seconds.

\[
\text{adapted MSET score} = \frac{\text{time longest subtask} - \text{time shortest subtask}}{\text{number of executed subtasks} - \text{rule breaks}}
\]  

(1)

Both the conventional BADS scoring method and the new index are based on the number of executed subtasks and the rule breaks. In addition to the conventional scoring method, this new scoring index takes the distribution of time spent on the six subtasks into account as well. A lower score indicates better planning performance and scores approximating zero indicate optimal performance.

Statistical analysis

Over the last decades, the assessment of reliability of tests has evolved. For example, reporting correlation coefficients between two tests does not take systematic changes in raw scores into account (Atkinson & Nevill, 1998; Flansbjer, Holmback, Downham, Patten, & Lexell, 2005; Rankin & Stokes, 1998; Weir, 2005). Therefore, in the present study we examined both test-retest reliability and parallel-form reliability using the guidelines for analyzing reliability of measurements in rehabilitation described by Lexell & Downham (2005). The intraclass correlation coefficients (ICC) (Shrout & Fleiss, 1979) were calculated using a 2-way random-effects ANOVA model (ICC_{2,1}). To detect systematic differences between the two test occasions, the mean differences (d) and bias 95% confidence intervals (CI) were calculated, where the multiplier 2 is derived from the t-table with 59 degrees of freedom (n-1, probability = 2.000).

A mean difference close to zero indicates no systematically better (or worse) performance on one of the test occasions (e.g., induced by a learning effect). Moreover, the limits of agreement (d ± 1.96 SD of the mean) (LOA) were computed and graphically presented in Bland-Altman plots (Bland & Altman, 1986). By plotting the difference scores against the mean scores of each pair of the adapted MSET scores, test agreement and systematic difference can be visualized. Next, the variability between the measurements was quantified, calculating the standard error of measurement (SEM) using Equation 2 (Liaw et al., 2008), where SD_{1,2} is the pooled SD of the two test occasions.

\[
\text{SEM} = \text{SD}_{1,2} \times \sqrt{1 - \text{ICC}}
\]  

(2)

Subsequently, SEM% was calculated by dividing the SEM by the mean of all measurements of both test occasions and multiplied by 100 (Lexell & Downham, 2005). Last, to determine whether (clinically) relevant differences between the test occasions may be present the smallest real difference (SRD) (Beckerman et al., 2001), the 95% SRD and the SRD% were determined. The SRD can be calculated by Equation 3.

\[
\text{SRD} = 1.96 \times \text{SEM} \times \sqrt{2}
\]  

(3)

Scores between two measurements exceeding the SRD indicate a clinical important change. The 95% SRD, the mean difference ± SRD, is a range to evaluate the amount of values outside the range, indicating real differences between test occasions. SRD% can be calculated by dividing the SRD by the maximum score of the test and multiplying by 100. Like the SEM%, the SRD% is independent of the units of measurements and thus more easily interpreted. A
SRD value lower than 10% of the possible highest score of the measurement, was considered as acceptable (Liaw et al., 2008; Lu, Chen, Huang, & Hsieh, 2012; Smidt et al., 2002). To examine the ecological validity of the adapted MSET Pearson’s correlation coefficients (r) between the EFI-NL and the MSET’ scores were computed. Analyses were conducted using IBM SPSS 19 for Windows (IBM corp., Armonk, NY) and Sigmaplot 12.5 (Systat Software Ink, San Jose, CA).

Results

Table 1 shows the demographic characteristics and scores on the adapted MSET and the EFI-NL questionnaire. Also, we examined the frequency of ceiling effects for the conventional scoring method of the MSET. Eighty percent of the participants gained the maximum raw score of 6 on parallel version 1 of the adapted MSET and 84 percent obtained this maximum score for parallel version 2. Note that the newly proposed scoring method only has a theoretical maximum score, and thus no ceiling performances were present.

Test-retest reliability

The ICC2,1 between T1 and T2 was 0.43 (p = .017). Although this score seems relatively low, it is within the limits of a fair relative test-retest reliability (Shrout & Fleiss, 1979). The mean difference (d) between the test occasions was -1.97 (SD 19.79), with a 95% bias CI of from-7.08 to 3.14, which was statistically not significant (t(59) = 1.39, p = .17) and an effect size (Cohen’s d) of 0.12, indicating no systematic differences between the scores on T1 and T2. Figure 1(A) shows the corresponding Bland-Altman plot. To evaluate the variability between the measurements the SEM was computed. The SEM was 12.37 and is an absolute value of the measurement error. The SEM% was 72.22, which indicates a high variability between the test scores. Subsequently, the SRD was 33.90 and the SRD% was 5.65%, showing that the SRD% is well within the acceptable range of 10%.

Parallel-form reliability

The ICC2,1 between version 1 and version 2 was .44 (p = .013). This is within the limits of a fair relative test-retest reliability (Shrout & Fleiss, 1979). The mean difference (d) between the test occasions was -3.51 (SD 19.57), with a 95% bias CI from -8.56 to 1.55, which was not significant (t(59) = 1.39, p = .17) and an effect size (Cohen’s d) of 0.21, indicating no systematic differences between the two versions. See Figure 1(B) for the Bland-Altman plot. The SEM% was 71.41%, which indicates a high variability between the test scores. Subsequently, the

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Participant characteristics and mean (SD) performance on EFI-NL and MSET.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>M (SD)</td>
</tr>
<tr>
<td>Male</td>
<td>16 (15.0)</td>
</tr>
<tr>
<td>Female</td>
<td>44 (15.0)</td>
</tr>
<tr>
<td>Age</td>
<td>31 (15.0)</td>
</tr>
<tr>
<td>Education level (mode (range))</td>
<td>6 (5-7)</td>
</tr>
<tr>
<td>NART-IQ</td>
<td>101.5 (9.1)</td>
</tr>
<tr>
<td>MSET</td>
<td></td>
</tr>
<tr>
<td>Version 1 raw score</td>
<td>5.6 (1.0)</td>
</tr>
<tr>
<td>Version 1 adapted score</td>
<td>18.8 (21.2)</td>
</tr>
<tr>
<td>Version 2 raw score</td>
<td>5.7 (0.7)</td>
</tr>
<tr>
<td>Version 2 adapted score</td>
<td>15.4 (9.3)</td>
</tr>
<tr>
<td>Appointment 1 raw score</td>
<td>5.7 (0.9)</td>
</tr>
<tr>
<td>Appointment 1 adapted score</td>
<td>18.1 (19.8)</td>
</tr>
<tr>
<td>Appointment 2 raw score</td>
<td>5.7 (0.7)</td>
</tr>
<tr>
<td>Appointment 2 adapted score</td>
<td>16.1 (12.1)</td>
</tr>
<tr>
<td>EFI-NL</td>
<td></td>
</tr>
<tr>
<td>Motivational Drive</td>
<td>15.0 (2.7)</td>
</tr>
<tr>
<td>Organization</td>
<td>17.5 (3.2)</td>
</tr>
<tr>
<td>Strategic Planning</td>
<td>23.3 (4.0)</td>
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<tr>
<td>Impulse Control</td>
<td>17.8 (3.2)</td>
</tr>
<tr>
<td>Empathy</td>
<td>24.5 (3.0)</td>
</tr>
<tr>
<td>Total Score</td>
<td>98.3 (9.1)</td>
</tr>
</tbody>
</table>

Notes. NART= National Adult Reading Test; Education level (1= less than primary school, 7= academic degree); MSET= Modified Six Elements Test; raw score and profile score are calculated according to BADS manual; EFI-NL= Executive Function Index-Dutch version.
Aim of this study was to investigate the reliability of an adapted version of the MSET, including a novel scoring method. While some reliability parameters were adequate, others were found to be insufficient for use in clinical practice. Specifically, the high variability in performance between the first and second administration affects the test-retest reliability. The adapted scoring method clearly reduced the occurrence of ceiling effects compared to the conventional scoring, even in a group of healthy participants and the parallel versions of the test are interchangeable, thus allowing measurement of executive functioning over the course of time. The adapted form of the MSET can be used before and after an intervention, without the bias of task specific learning effects.

The intraclass coefficient (ICC) is the most frequently used reliability measure. However, a generally accepted ICC “cut-off” score has not been defined. It is recommended that ICC values above .75 represent “excellent reliability” and values between .4 and .75 represent “fair to good reliability” (Fleiss, 1986). The ICC values for both for test-retest reliability and for parallel form reliability were merely within the fair range indicating modest reliability. The low ICC values could also reflect the homogeneous character of the participants (Lexell & Downham, 2005), therefore evaluation of other reliability measures was warranted. Next, the systematic changes between the test occasions were assessed, the Bland-Altman plots did not reveal any systematic differences between the adapted MSET scores on the two test occasions. While there were no systematically higher scores on one of the two versions or one of the two test moments, a relatively high variability was found. Although there is no consensus about the interpretation of the SEM statistic and which boundaries are acceptable (Atkinson & Nevill, 1998), our reported SEM percentages are clearly too high, affecting the test’s reliability. This high variability may be due to the used scoring index, in which the distribution of time over the MSET subtasks contributed to the obtained scores. Participants may not always show a similar distribution of time on two subsequent test occasions. Optimizing the distribution of time seems, however, an important aspect of planning ability and hence a valuable contribution to the MSET. Still, the high variability questions the applicability of time distribution in scoring the MSET. Other studies examining executive tasks also reported large variability in cognitive performance (Pietrzak et al., 2008). Another possible explanation is the complex nature of executive tests, due to involvement of multiple cognitive processes, making executive tests susceptible to performance variability (Calamia, Markon, & Tranel, 2013; Delis, Kramer, Kaplan, & Holdnack, 2004). The smallest real difference (SRD) was used to determine if the adapted MSET allows the detection

![Bland-Altman plots](image)

**Figure 1** Bland-Altman plots for test-retest reliability (A) and for parallel form reliability (B). The differences between the 2 measurements (T2 minus T1 for test-retest reliability; version 2 minus version 1 for parallel form reliability) are plotted against the means of the 2 measurements. The solid lines show the mean difference ($d$) and the dashed lines show the limits of agreement.

**Ecological validity and correlation with education/IQ**

Correlations (Pearson’s $r$) between the MSET and EFI-NL were computed as an estimate of the test’s ecological validity. All $r$-values between the mean raw MSET scores and the EFI scores were below .25 (p-values > .057). Absolute $r$-values between the mean adapted MSET scores and the EFI scores were below .14 (p-values > .27). For both the raw and the adapted MSET scores weak to moderate correlations were found with educational level ($r = .46$, $p = .001$ for the raw score; $r = .31$, $p = .017$ for the adapted score). Neither estimated IQ nor age correlated significantly with the MSET scores (all absolute $r < .25; p > 0.054$).
adaptation. Shallice and Burgess (1991) describe that the aim of the original SET task, as was done in the BADS-C (Emslie et al., 2003) as well, seems a considerable Next to the scoring index, the replacement of the dictation task by a sorting in clinical practice.

Therefore a feasible tool to assess executive functioning over the course of time (Smidt et al., 2002), indicating that MSET is useful to detect changes and is versions (version 1 and version 2), were well within the range of 10% or less between the test administrations (T1 and T2) and the scores between the parallel of substantial ‘real’ change in individuals. The SRD%, for both the scores between the test administrations (T1 and T2) and the scores between the parallel versions (version 1 and version 2), were well within the range of 10% or less (Smidt et al., 2002), indicating that MSET is useful to detect changes and is therefore a feasible tool to assess executive functioning over the course of time in clinical practice.

Next to the scoring index, the replacement of the dictation task by a sorting task, as was done in the BADS-C (Emslie et al., 2003) as well, seems a considerable adaptation. Shallice and Burgess (1991) describe that the aim of the original SET is to evaluate if a participant is able to devise a simple plan, scheduling the subtasks, which are ‘fairly simple’ activities, efficiently and keeping a check on the time. The main objective is to evaluate the application of the strategy between the tasks (switching without rule breaks), results within subtasks are not taken into account. Therefore, changing the subtask with another simple task has only marginal effect on the construct and interpretation of the test. This was confirmed in a previous study (Bertens et al., 2014) where the adapted MSET was administered in brain-injured patients and significantly correlated with four of six other executive tests. The adaptation contributes to the suitability of the test for patients with language disorders (due to e.g., brain injuries, autism). Moreover, conventional tape recorders, used for the conventional dictation task, have become increasingly obsolete and digital recording methods are less uniform and more complicated to operate. Also, patients may feel embarrassed when prompted to produce details about their personal lives during this task (Gouveia et al., 2007), resulting in a brief amount of time spent on this subtask.

Many studies investigated to what extent neuropsychological tests predict everyday functioning. The results of several studies show that the relationship between executive tasks and measures of everyday functioning are moderate to weak (Alderman, Burgess, Knight, & Hemman, 2003; Bogod, Mateer, & MacDonald, 2003; Norris & Tate, 2000). The Tower of London Test (Shallice, 1982) is generally considered as a test of planning. However, next to a questionable construct validity (Burgess et al., 2006), its relevance to everyday planning could not be established (Goel, Grafman, Tajik, Gana, & Danto, 1997). The BADS aimed at measuring executive functioning in a more ecologically valid way. A previous study confirmed that the MSET, one of the subtests of the BADS, was able to predict everyday executive functioning, suggesting that it is an ecologically valid tool (Renison, Ponsford, Testa, Richardson, & Brownfield, 2012). Nonetheless, in the present study we did not find significant correlations between the MSET and the self-report questionnaire, the EFI-NL. The EFI was developed to measure the different aspects of executive function in healthy individuals (Spinella, 2005). Unfortunately, there are few studies using this index and comparisons with other well established questionnaires are lacking as yet. A recent study by Janssen (2014) also demonstrated modest to weak correlations between the EFI-NL and a measure of fluid intelligence (Kaufman Adolescent and Adult Intelligence Test; Kaufman & Kaufman, 1993) which highly overlaps with executive function, in a mixed psychiatric sample. However, discrepancies between neuropsychological test scores and self-report measures are commonly observed (D. Chan, 2009). It is suggested that these assessment strategies tend to tap different aspects of the same phenomena as is seen in studies on subjective cognitive functioning (Gervais et al, 2009). This is further supported by evidence showing that the MSET correlates low with self-reported daily executive functioning compared to ratings by significant others (Wilson et al., 1996).

A limitation of the study is that only healthy participants were included. This group of participants was rather homogeneous (e.g., highly educated, relatively young age). This may have affected the results (e.g., contributed to the low ICC values). Although it was not the aim of this study, inclusion of healthy participants makes it not possible to investigate the test’s validity as this sample has no executive dysfunction in the clinical sense. Another limitation is that we did not compare the adapted MSET to the ‘standard’ MSET. Although we assume that changing the content of the subtasks does not affect the test’s construct, this cannot be completely ruled out. A next step is to collect normative data in which the distribution of time over the subtasks is recorded as well. The new subtasks only require marginal adjustment of the conventional BADS instructions. The sorting task materials can be obtained in hardware stores. More details regarding the test materials can be obtained from the corresponding author.

In conclusion, the present study shows that the adapted MSET, including the two versions and the proposed scoring method, is capable of detecting real changes. Between the two parallel versions no systematic difference were observed, indicating that both parallel versions of the test are interchangeable and therefore suitable for both scientific research and clinical practice. However, other reliability measures, such as the observed high variability between test scores question the feasibility and reliability of the proposed scoring index. The previously established ecological validity of the test was not confirmed.
Three Validity of an adapted scoring method for a Modified Six Elements Test in individuals with brain injury

Published as:
Abstract

The Modified Six Elements Test assesses several executive functions, including planning, self-monitoring, and task-switching. The present study examines whether an adapted scoring method is appropriate for discriminating between brain-injured persons with and without executive deficits. A Modified Six Elements Test was administered to 70 participants with acquired brain injury in the chronic phase. The group was divided into individuals with and without executive impairments based on several other executive tests. The discriminative value for both the conventional raw score and the adapted scoring method was evaluated using Receiver Operating Characteristic (ROC) analyses. Both scoring methods discriminated significantly between persons with impaired and unimpaired executive functions (raw score: AUC=0.703, p=.004; adapted score: AUC=0.780, p=.000). Only the adapted scoring method proved sensitive (81%) and specific (67%) within a clinically useful range. Within this range an acceptable cut-off score could be determined. Altogether, the proposed Modified Six Elements Test scoring index is a potentially clinically useful contribution to the measurement of executive functions.

Introduction

Brain-injured persons with executive deficits often have difficulties in formulating and achieving goals due to deficits in planning and strategy application (Damasio, 1995; Duncan, Emslie, Williams, Johnson, & Freer, 1996; Lezak, 1982; Levine et al., 2000; Stuss & Levine, 2002). As a consequence, unusual and unstructured situations become particularly difficult to handle. However, most neuropsychological tests consist of structured and closed tasks, making reliable assessment of executive functions challenging. A widely used test to assess executive functions is the Behavioural Assessment of the Dysexecutive Syndrome (BADS; Wilson, Alderman, Burgess, Emslie, & Evans, 1996). The aim of this test battery is to assess executive problems in a way that simulates aspects of daily living, by using unstructured and open tasks. The BADS consists of six subtests, measuring different executive processes. One of these subtests is the Modified Six Elements Test (MSET), a measure of multitasking ability in which multiple skills such as planning, working memory, prospective memory, rule learning, strategy application, and response monitoring are involved.

The MSET has proven to be a good predictor for problems with planning and goal-directed behavior (Alderman, Burgess, Knight & Henman, 2003; Burgess, Alderman, Evans, Emslie, & Wilson, 1998) and has consistently been found to be one of the most sensitive subtests of the BADS (Bennett et al., 2005; Burgess et al., 1998). Renison, Ponsford, Testa, Richardson, and Brownfeld (2012) found that the MSET could reliably predict everyday executive performance in individuals with traumatic brain injury, suggesting that the MSET is an ecologically valid tool. Everyday executive difficulties were measured with the Dysexecutive Questionnaire (DEX; Wilson et al., 1996), a 20-item checklist in which cognitive, behavioral, and emotional aspects of executive difficulties were reported by both participants and independent raters. In a recent study, Emmanouel, Kessels, Mouza and Fasotti (2014) showed that the MSET was the most sensitive subtest of the BADS in discriminating between individuals with anterior and posterior lesions. The MSET has been used in various patient groups with different brain disorders in order to evaluate executive functions, for example, persons with MCI and Alzheimer’s dementia (Espinosa et al., 2009), post-concussive symptoms (Chan, Hoosain, Lee, Fan, & Fong, 2003), substance abuse (Fernandez-Serrano, Perez-Garcia, Schmidt Rio-Valle, & Verdejo-Garcia, 2010), schizophrenia (Liu et al., 2011) and traumatic brain injury (Bennett, Ong, & Ponsford, 2005; Chan & Manly, 2002; Manly, Hawkins, Evans, Woldt, & Robertson, 2002).

The MSET (Wilson et al., 1996) consists of three tasks (simple arithmetic, written picture naming, dictation), each of which consists of two parts (subtask A...
and B). Participants are instructed that they have ten minutes to work on at least a part of each of these six subtasks. However, they are also told that it is not allowed to switch between two parts (subtasks) of the same task. Thus, a participant is not allowed to switch from subtask A of the arithmetic task directly to subtask B of arithmetic, as first one of the other tasks, written picture naming or dictation, has to be dealt with (Burgess et al., 1998). This rule requires participants to engage in task switching (i.e., multitasking) throughout the test. An advantage of the MSET compared to other conventional executive function tests is its highly unstructured character. Therefore, it requires a considerable amount of planning and monitoring behavior. However, the MSET has some limitations as well. Raw scores have a limited range from 0-6 and the standardized profile scores, obtained in accordance with the manual of the BADS, range from 0-4. In previous studies using the MSET, brain-injured persons obtained mean profile scores of 3 or more (Gouveia, Brucki, Malheiros, & Bueno, 2007; Manly et al., 2002). Individuals with mild executive deficits easily perform at maximum level, indicating that mild executive impairments are not detected by the MSET due to ceiling effects. Furthermore, the dictation task of the MSET requires the use of a tape recorder to record a personal story of the participant. Conventional tape recorders are not only becoming increasingly obsolete, participants have also reported to feel embarrassed by talking about personal topics during this task (Gouveia et al., 2007).

In a recent study (Bertens, Fasotti, Egger, Boelen, & Kessels, 2014), the reliability of an adapted version of the MSET was examined in 60 healthy participants. In the MSET, the dictation subtask was replaced by a sorting task. Moreover, a revised scoring method was proposed, in which the distribution of time spent on the subtasks was taken into account as well. Also, a parallel version of the MSET was added, allowing the measurement of executive functions over the course of time. The test-retest- and parallel form reliability were found to be adequate. However, the validity and diagnostic utility of the adapted scoring method in brain-injured individuals has not been investigated yet. Here, we examine the diagnostic utility of a recently proposed scoring method (Bertens et al., 2014) of a MSET in persons with brain injuries. Moreover, the adapted scoring method will be compared to the conventional scoring method as proposed in the BADS (Wilson et al., 1996). We also examine to what extent these scoring methods discriminate between individuals with and without executive deficits, based on their performance on other well established executive tests. Although this comparison does not investigate the test's ecological validity, that is, its relation with everyday executive problems, our study allows a direct comparison of the sensitivity and specificity of both scoring methods. Furthermore, with the newly proposed scoring method, we aim to reduce ceiling effects, a highly relevant issue in clinical practice. In addition, the convergent validity of both scoring methods will be examined by calculating their correlations with other executive tests.

**Methods**

**Participants**

The data of the seventy participants who were included in the current study were collected as part of the recruitment procedure for a larger treatment study, approved by the Medical Review Ethics Committee region Arnhem-Nijmegen (Bertens, Fasotti, Boelen, & Kessels, 2013). All participants had an acquired brain injury (ABI) of non-progressive nature, such as traumatic brain injury, stroke or hypoxia. Minimal time since onset of the injury was 3 months. Other eligibility criteria were age between 18 and 70 years, living independently at home and being fluent in the Dutch language. Participants were recruited from the outpatient department of the Rehabilitation Medical Centre Groot Klimmendaal in Arnhem, the Netherlands and the outpatient rehabilitation clinic for brain injured individuals and the department of Neuropsychiatry of the Sint Maartenskliniek in Nijmegen, the Netherlands. Exclusion criteria were the presence of severe psychiatric problems; substance abuse (current or in the past); neurodegenerative disorders; severe cognitive comorbidity (e.g., aphasia, dementia). Recruitment was based on assessment by clinicians of the participating centres who excluded all potential participants not meeting the above mentioned criteria. Executive function-ins were assessed using six other traditional executive tests.

Table 1 shows the demographic characteristics of the participants. All participants were Caucasian. Level of education was rated using seven categories based on the Dutch educational system, ranging from 1 (less than primary school) to 7 (university degree) (Duets & Kessels, in press). For descriptive purposes, these levels of education were converted to years of education, as is customary in the Anglo-Saxon world (See also Hochstenbach, Mulder, Van Limbeek, Donders & Schoonewaldt, 1998).

**Neuropsychological tests**

The conventional MSET, a subtest of the executive test battery Behavioural Assessment of the Dysexecutive Syndrome (BADS) consists of three open-ended tasks, namely simple arithmetic, dictation and written picture naming. Each of these tasks consists of two parts (subtask A and B). Participants are instructed to execute at least a part of each of these six subtasks within 10 minutes.
The discriminative value of the MSET for executive deficits was evaluated by calculating Receiver Operating Characteristic (ROC) curves for both the raw score and the adapted score separately. The Area Under the Curve (AUC) indicates the discriminative power of the test, which varies between 0.5 (no discriminative power) to 1.0 (maximum discriminative power). Within this analysis of covariance was performed when applicable. To control for possible effects of demographic differences a multivariate analysis of variance (general linear model) was performed to compare the performance on the MSET between the two groups (executively impaired, executively intact), with both demographic characteristics between the groups, t-tests or nonparametric tests for nominal or ordinal variables (sex distribution and education level) were conducted. To control for possible effects of demographic differences a multivariate analysis of variance was performed. For statistical analyses IBM SPSS 20.0 was used. Alpha was set at 0.05 for all analyses and two-tailed tests were used. A multivariate analysis of variance (general linear model) was performed to compare the performance on the MSET between the two groups (executively impaired, executively intact); with both the raw and adapted MSET scores as dependent variables. To compare the demographic characteristics between the groups, t-tests or nonparametric tests for nominal or ordinal variables (sex distribution and education level) were conducted. To control for possible effects of demographic differences a multivariate analysis of covariance was performed when applicable.

However, it is not allowed to switch between two subtasks of the same type. In the adapted MSET that was used in the present study, the dictation task was replaced by a sorting task in which plastic wall plugs (part A) and small cable ties (part B) had to be sorted by color (three colors) (Bertens et al., 2014). The test was administered according to the instructions of the Dutch version (Krabbendam & Kalf, 1998) of the BADS test manual. The total administration time was approximately 15 minutes (5 minutes for the instructions and 10 minutes for the execution). For each participant, the number of executed subtasks and the rule breaks were scored, as well as the amount of time spent on each subtask. By subtracting the rule breaks from the number of executed subtask raw scores were obtained (range 0-6), that were also converted into profile scores (range 0-4) in agreement with the manual of the BADS. In addition, an adapted scoring method was calculated aimed at reducing ceiling effects in mildly impaired individuals (Bertens et al., 2014) using the following formula:

\[
\text{adapted MSET score} = \frac{\text{time longest subtask(sec)} - \text{time shortest subtask(sec)}}{\text{number of executed subtasks} - \text{rule breaks}}
\]

If the number of rule breaks is equal to or exceeds the number of executed subtasks, the denominator’s value is set to 1 (i.e., the denominator can never be 0 or a negative number). This scoring index takes into account the distribution of time spent on the six subtasks by subtracting the shortest time spent on one of the six subtasks (i.e., the total time spent on the subtask) from the longest time spent on one of the six subtasks (i.e., the total time spent on the subtask). A more uniform distribution of time across the tasks indicates better multitasking abilities. A lower score indicates better planning performance.

In addition to the MSET, six other neuropsychological tests were administered to assess the main subdomains of executive function (Lezak, Howieson, Bigler, & Tranel, 2012). To assess planning, the Zoo Map test (subtest of BADS) was administered. **Response generation** was measured with the Category Fluency test (CFT) and the Letter Fluency test (LFT). **Response inhibition** was assessed with the Go/No-go task from the computerized TAP 2.1 (Zimmermann & Fimm, 2007). The Brixton Spatial Anticipation test (Burgess & Shallice, 1997) was utilized to measure **task switching** and Letter-Number Sequencing (LNS; subtest of WAISIII; Wechsler, 1997) was administered to assess working memory. Scores on the tests were expressed in various standardized scores (i.e., percentile scores, T-scores), in agreement with the respective test manuals. All tests were administered by trained test assistants.

### Procedure and analyses

Based on six executive tests, the participants were divided into an executively impaired group and an executively unimpaired group. The criteria for executive impairments were: a standard score of 1.5 SD below the normative mean on at least two of the executive tests or a standard score between 1 and 1.5 SD below the normative mean on at least four of these tests or a standard score of 1.5 SD below the normative mean on one executive test and a standard score between 1 and 1.5 SD below the normative mean on at least 2 of the remaining executive tests (Bertens et al., 2013).

For statistical analyses IBM SPSS 20.0 was used. Alpha was set at 0.05 for all analyses and two-tailed tests were used. A multivariate analysis of variance (general linear model) was performed to compare the performance on the MSET between the two groups (executively impaired, executively intact); with both the raw and adapted MSET scores as dependent variables. To compare the demographic characteristics between the groups, t-tests or nonparametric tests for nominal or ordinal variables (sex distribution and education level) were conducted. To control for possible effects of demographic differences a multivariate analysis of covariance was performed when applicable.

Table 1 Characteristics of the participants with and without executive impairments.

<table>
<thead>
<tr>
<th></th>
<th>Executively impaired group</th>
<th>Executively unimpaired group</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>31</td>
<td>39</td>
</tr>
<tr>
<td>Age (mean (SD))</td>
<td>51.7 (±10.8)</td>
<td>47.5 (±14.3)</td>
</tr>
<tr>
<td>Sex (N male/female (%))</td>
<td>17/14 (55%/45%)</td>
<td>25/14 (64%/36%)</td>
</tr>
<tr>
<td>Education level (mode (range)) **</td>
<td>5 (3-7)</td>
<td>5 (4-7)</td>
</tr>
<tr>
<td>Education (years) (mean (SD)) *</td>
<td>11.8 (±3.1)</td>
<td>14.3 (±3.4)</td>
</tr>
<tr>
<td>Time past brain injury (months) (mean/median (SD; range))</td>
<td>34.1/15.0 (±23.1; 4-324)</td>
<td>19.5/11.5 (±67.0; 3-89)</td>
</tr>
<tr>
<td>Etiology (N) (TBI/stroke/other (%))</td>
<td>8/22/1 (26%/71%/3%)</td>
<td>13/24/2 (33%/62%/5%)</td>
</tr>
</tbody>
</table>

Notes. * p<0.01; **p<0.001
analysis an optimal cut-off point was determined, fulfilling the criteria of a good sensitivity (>80%) and an acceptable specificity (>60%) rate (see Blake, McKinney, Treece, Lee, & Lincoln, 2002; Kessels, Mippen, Melis, & Rikkert, 2009; Oosterman, Molenveld, Olde Rikkert, & Kessels, 2010).

To examine the convergent validity of the MSET and the other executive tests, Pearson correlation coefficients (r) were calculated between both the raw and the adapted scores of the MSET and the other executive tests. For this analysis, the scores of the other executive tests were expressed in raw scores, with higher scores indicating better test performance. For this reason, the scores on the Brixton were expressed in number of correct items instead of errors, whereas the scores on the Go/No-go task were multiplied by -1.

Results

Based on the six executive tests the participants were divided into an executively impaired group (N=31) and an executively unimpaired group (N=39). Intergroup comparisons showed no significant difference for age [F(1,68)=1.36; p=0.18], but a significant difference for education level [F(1,336.00)=336.00; p=0.001] and years of education [t(68)=3.26; p=0.002]. No differences between the groups with respect to post onset time [t(42)=0.97; p=0.34] and sex distribution were present [χ²(1)=0.62; p=0.43].

Table 2 shows the MSET scores for both the executively impaired and unimpaired groups. Significant differences on the MSET scores between the executively impaired group and the executively unimpaired group were found [F(2,67)=6.30; p=0.003], with the executively impaired group performing worse than the executively unimpaired group (as reflected by a lower raw score and a higher adapted score). These group differences were found for both the raw scores [F(1,68)=9.72; p=0.003] with a moderate to large effect size (Cohen’s d=0.71) and the adapted MSET scoring method [F(1,68)=11.85; p=0.001] with a moderate to large effect size (d=0.79). As educational levels differed significantly between the groups, a multivariate analysis of covariance was conducted with education level as covariate. This analysis showed that education level [F(2,66)=1.11; p=0.34] did not contribute significantly, and the overall group differences remained statistically significant [F(2,66)=7.20; p=0.001].

The discriminative value of both scoring methods was evaluated using ROC analyses. The ROC graph of the raw MSET score as predictor of executive function deficits showed a significant area under the curve (AUC=0.70; p=0.004; Figure 1a). However, no optimal cut-off score with a sensitivity of >80% and a specificity of >60% could be determined (Table 3). Moreover, a ROC curve with an AUC ≤0.75 is generally interpreted as clinically not useful (Fan, Upadhye, & Worster, 2006). The ROC analysis of the adapted MSET score, as a predictor for executive deficits, also showed a significant Area Under the Curve (AUC=0.78; p=0.000; Figure 1b). Moreover, for this scoring index it was possible to determine an optimal cut-off score (18.63) with a sensitivity of 81% and a specificity of 67%, indicating that a score of 18.63 or more is an indication for executive deficits (Table 4). Statistical comparison between the areas under the ROC curves of both scoring indices (Hanley & McNeil, 1982) did not show a significant difference between the AUCs (p=0.35).
impaired’ group (n=31) and 30 in the ‘unimpaired’ group (n=39). The most frequently found score in both groups was the maximum score. The maximum adapted MSET score (reflecting an equal distribution of time spent on all 6 tasks without any rule breaks) is 0, a score which was not achieved by any of the participants. For the 41 participants who obtained the maximum raw score, the adapted MSET scores ranged from 2 to 51 (mean score 15.8; SD 10.2) indicating an improved variability and no ceiling effect.

With respect to the convergent validity of both scoring methods, an expected high negative correlation was found between the raw and the adapted MSET scores, r = 0.745, p < 0.01, in which higher raw scores and lower adapted scores represent better test performance. Correlations between both scoring methods of the MSET and the other executive tests are reported in Table 5. Both scoring indices showed a similar pattern. That is, for the raw score significant, but moderate (cf. Cohen, 1992) correlations were found with three out of six executive function tests. Four of the six tests correlated significantly with the adapted score, also in the moderate range.

Finally, we examined the occurrence of ceiling effects by examining the frequency of participants who obtained the maximum score. Table 6 shows the distribution of the raw MSET scores, followed by the statistics of the corresponding adapted MSET scores. Forty-one of seventy participants had a maximum raw score of 6 (equivalent to a maximum profile score of 4), 11 of whom were in the impaired’ group (n=31) and 30 in the ‘unimpaired’ group (n=39). The most frequently found score in both groups was the maximum score. The maximum adapted MSET score (reflecting an equal distribution of time spent on all 6 tasks without any rule breaks) is 0, a score which was not achieved by any of the participants. For the 41 participants who obtained the maximum raw score, the adapted MSET scores ranged from 2 to 51 (mean score 15.8; SD 10.2) indicating an improved variability and no ceiling effect.

<table>
<thead>
<tr>
<th>Raw MSET score</th>
<th>N</th>
<th>Mean (SD)</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1</td>
<td>13.9</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>5</td>
<td>110.1</td>
<td>37-211</td>
</tr>
<tr>
<td>3</td>
<td>9</td>
<td>64.2</td>
<td>30-110</td>
</tr>
<tr>
<td>4</td>
<td>7</td>
<td>51.3</td>
<td>19-93</td>
</tr>
<tr>
<td>5</td>
<td>7</td>
<td>27.5</td>
<td>21-39</td>
</tr>
<tr>
<td>6</td>
<td>41</td>
<td>15.8</td>
<td>2-51</td>
</tr>
</tbody>
</table>
Discussion

The aim of this study was to examine the diagnostic utility of an updated version of the MSET (Bertens et al., 2014) including an adapted scoring method. The results show that persons with executive function deficits performed significantly worse on the MSET than persons without executive deficits, regardless of scoring method. With respect to the discriminative value, the AUCs for the raw score and the adapted score were both statistically significant. Although the AUCs did not significantly differ, only the AUC for the adapted score was within a clinically useful range (Fan, Upadhye, & Worster, 2006). An acceptable cut-off score, fulfilling the criteria of having a good sensitivity and an adequate specificity for discriminating between impaired and normal executive function, could only be determined for the adapted score.

An altered version of the MSET was used in which the dictation subtask was replaced by a sorting task, making the test more suitable for individuals with language impairments. Shallice and Burgess (1991) described that the aim of the original SET was to evaluate if a participant could devise a simple plan, scheduling the subtests (consisting of 'fairly simple' activities) efficiently and keeping a check on time. The main objective was to evaluate the application of an efficient strategy to alternate between the tasks (switching without rule breaks). Results within subtasks are not taken into account. Therefore, changing a subtask for another simple task should have marginal effect on the construct of the test. Moreover, the dictation task is also replaced by a sorting task in the BADS-C, the children's version of the BADS (Emslie et al., 2003).

The compatibility between both MSET scoring indices and other executive tests is acceptable. For the adapted scoring method, significant correlations were found with four out of six executive tests, however these correlations were weak to moderate. No correlations were found between the MSET and the Zoo Map test, measuring planning (see also Oosterman, Wijers and Kessels, 2013) and the Brixton Spatial Anticipation Test, measuring shifting. Although planning and shifting may seem important aspects, the aim of the MSET was to measure executive functions in an ecologically validity way using unstructured and open-ended tasks which better mimics everyday demands. This may explain the low to moderate and even absent correlations between the MSET and traditional more structured executive tests.

A limitation of the current study is that the executive tests used to divide the participants in an executively impaired and executively intact group, were traditional executive tests. As a result, we cannot conclude that our revised scoring method also optimizes the test’s ecological validity. One could argue that a comparison with other ecologically valid (e.g., open ended tasks which resemble real life duties) tasks is required to determine the convergent validity of the MSET. Examples of such tasks are the Executive Secretarial Task (Lamberts, Evans & Spikman, 2010), the Multiple Errands Test (Alderman et al., 2003) and the Hotel Task (Manly et al., 2002). However, although these tasks are standardized assessment procedures, their psychometric properties (e.g., sensitivity and specificity) have not been examined thoroughly and normative data are not available. More importantly, administration of these tests is very time consuming and may last several hours. Therefore, these paradigms are less suitable for implementation in clinical practice (see also Lamberts et al., 2010).

Future studies should further examine which executive aspects the MSET is tapping. Moreover, the ecological validity of the proposed scoring method should be further investigated by including questionnaires such as the Dysexecutive Questionnaire (Wilson et al., 1996) or the Executive Function Index (EFI; Spinella, 2005) that assess everyday executive difficulties or by using established everyday executive function tests. The validity of the adapted scoring method should be investigated in other clinical populations as well. Another limitation of our study is that other cognitive domains were not assessed. Therefore we cannot rule out that the two groups also differed on memory or attention performance. Eventual differences could have influenced the results on the executive function tasks, including the MSET.

To our knowledge, this is the first study investigating the MSET taking the aspect of time distribution into account. The conventional scoring method as described in the manual of the BADS only includes a penalty profile point when individuals spend more than 271 seconds on one of the MSET subtasks (Wilson et al., 1996). It lacks a scoring system for unequal time distribution throughout the subtests. In order to equally distribute the allowed time over the six subtests, planning behavior and time monitoring are required (Mantyla, Carelli, & Forman, 2007). In the current study time distribution was assessed by subtracting the shortest time spent on a subtask from the longest time spent on a subtask. Unfortunately, this method does not take into account the overall variability of time spent on the subtasks. However, it is a relatively simple method to estimate time distribution and feasible in clinical practice. Adding the aspect of time distribution to the scoring index prevents the occurrence of ceiling effects in persons with mild executive deficits. This improvement is indicated by the better sensitivity of the adapted MSET score (resulting in a clinically useful cut-off point) compared to the poor sensitivity of the traditional score. An unintended outcome of this study was that the two investigated groups differed significantly on some demographic characteristics. The impaired group had a lower education level, which may affect performance on the executive tests. However adjusting for this potentially confounding factor did not alter the results.
In conclusion, the present study shows that the adapted scoring method of the MSET can be clinically useful in measuring executive deficits in individuals with brain injuries, and more sensitive and specific than the conventional score. The adapted scoring method of the MSET is able to discriminate between persons with and without executive function deficits. The next step is to collect normative data in a sample of healthy participants from various age groups and the full spectrum of educational levels, for use in clinical assessment. Although the MSET, including the adapted scoring index, may be clinically useful as a first executive screening or as a treatment outcome measure, it is always advised to use multiple tests for the assessment of executive functions, since executive function is a multifarious concept.
Four Errorless Goal Management Training: study rationale and protocol

Published as:
Abstract

Many brain-injured patients referred for outpatient rehabilitation have executive deficits, notably difficulties with planning, problem-solving and goal directed behaviour. Goal Management Training (GMT) has proven to be an efficacious cognitive treatment for these problems. GMT entails learning and applying an algorithm, in which daily tasks are subdivided into multiple steps. Main aim of the present study is to examine whether using an errorless learning approach (preventing the occurrence of errors during the acquisition phase of learning) contributes to the efficacy of Goal Management Training in the performance of complex daily tasks. The described study protocol comprises an assessor-blind randomized controlled trial, in which the efficacy of Goal Management Training with an errorless learning approach will be compared with conventional Goal Management Training, based on trial and error learning. In both conditions 32 patients with acquired brain injury of mixed etiology will be examined. Main outcome measure will be the performance on two individually chosen everyday-tasks before and after treatment, using a standardized observation scale and goal attainment scaling. This is the first study that introduces errorless learning in Goal Management Training. It is expected that the GMT-errorless learning approach will improve the execution of complex daily tasks in brain-injured patients with executive deficits. The study can contribute to a better treatment of executive deficits in cognitive rehabilitation.

Background

Brain-injured patients referred for outpatient rehabilitation frequently experience difficulties with planning, problem solving, reasoning and goal directed behaviour (Baddeley & Wilson, 1994; Lezak, Howieson, & Bigler, 2012; Stuss & Levine, 2002). These difficulties can be characterized as executive deficits (Baddeley & Wilson, 1994; Burgess, Veitch, de Lacy Costello, & Shallice, 2000; Damasio, 1995; Shallice, 1982) and compromise daily functioning and even functional independence (Levine et al., 2000; McDonald, Flashman, & Saykin, 2002). More specifically, dysfunction of these higher-level control processes leads to real-life everyday disorganization (Mateer, Sohlberg, & Crinean, 1987) and even subtle executive deficits often provoke difficulties in the performance of everyday-life tasks (Boelen, Spikman, Rietveld, & Fasotti, 2009). Because of the high prevalence of executive dysfunction in the brain-injured population (Levine et al., 2007) and its considerable impact on everyday life, effective treatment is warranted.

Goal Management Training

Based on Duncan’s (1996) theory of goal neglect, Robertson (1996) developed Goal Management Training (GMT). GMT is a rehabilitation technique aimed at helping patients with executive impairments to better structure (instrumental) activities of daily living (i)ADL. GMT entails learning and applying an algorithm, in which complex tasks are subdivided into multiple task steps. Both, the final goal and the task steps leading to this goal have to be kept active in working memory. Unfortunately, working memory processes are often impaired in patients with executive deficits. Monitoring goal-directed behaviour and the correct execution of task steps are the main aims of GMT. GMT can be applied to (re)learn all sorts of (i)ADL tasks, for example cleaning up the living room, processing and organizing mail or making a day schedule. In figure 1 both the GMT algorithm and an example of its application are illustrated. Previous studies have established the efficacy of GMT (Fish et al., 2007; Grant, Ponsford, & Bennett, 2012; Levine et al., 2000; Levine et al., 2007; Levine et al., 2011; Van Hooren et al., 2007) and the training is widely applied in the field of cognitive rehabilitation. The acquisition of the algorithm and the performance of the task steps, however, relies on self-control, which is impaired in patients with executive problems (Burgess & Simons, 2005; Shallice, 1982). Consequently, errors that occur during the acquisition of the algorithm and the learning of the task steps are not corrected and may interfere with the correct acquisition of the GMT process and the correct performance of the task (Baddeley, 1992). Preventing the occurrence of errors during learning, also known as errorless learning, may enhance treatment effects.
Errorless learning in Goal Management Training

In errorless learning, the occurrence of errors during the learning phase is prevented in contrast to standard learning, or trial and error learning, in which errors may occur naturally. Fillingham, Sage, and Ralph (2005) described the mechanism of errorless learning using the Hebbian learning model (Hebb, 1961). Learning is described as a strengthening of the connection between neurons that fire together. If a stimulus is followed by a response, the subsequent pattern of neural activity will be more likely to be activated again in similar situations. This means that the same response can be expected, even if it is an incorrect action (McClelland, Thomas, McCandliss, & Fiez, 1999). If an errorless learning approach is applied in this process, the activation of incorrect neural patterns will be prevented and erroneous actions will not be evoked.

In clinical practice, several errorless learning techniques can be applied during training of complex daily tasks. Task steps can be taught using cue cards, (feed-forward) verbal instructions and visual demonstration or modeling by the trainer (Kern et al., 2009; Voigt-Radloff, Leonhart, Olde Rikkert, Kessels, & Hull, 2011; Wilson, Baddeley, Evans, & Shiel, 1994). Several studies have shown that the quality of task performance after errorless learning is superior compared to errorful learning in patients with cognitive impairments of different aetiologies (Clare & Jones, 2008; Dechamps et al., 2011; Ehlhardt et al., 2008; Haslam, Hodder, & Yates, 2011; Kessels & De Haan, 2003; Kessels & Olde Hensken, 2009; Mount et al., 2007). Most studies on errorless learning have focussed on patients with memory deficits. In these studies the efficacy of errorless learning is explained by the mechanism that errors are not consciously corrected because of impairments in explicit memory, but implicitly consolidated through a relatively intact implicit memory system (Baddeley & Wilson, 1994; Kessels, Boekhorst, & Postma, 2005; Kuzis et al., 1999). However, other studies do not agree with this hypothesis and describe the benefits of errorless learning by residual explicit memory processes (Hunkin, Squires, Parkin, & Tidy, 1998; Tailby & Haslam, 2003). Another mechanism that may explain the advantage of errorless learning in patients with executive disorders is that errors are not detected due to a failing error-monitoring system (Bettcher, Giovannetti, Macmullen, & Libon, 2008; Yochim, Baldo, Kane, & Delis, 2009) and the inability to adjust behaviour on the basis of feedback (Clare & Jones, 2008). By preventing the occurrence of errors in learning the execution of a task, both these systems are circumvented.

The main aim of the current study is to examine the efficacy of Goal Management Training using an errorless learning approach in the treatment of executive impairments in patients with acquired brain injury, focusing on (instrumental) activities of daily living ((i)ADL). Both GMT and errorless learning are two well investigated instructional methods of proven effectiveness. However, to date they have never been combined. Using an errorless learning approach in GMT may optimize both the acquisition of the GMT algorithm and the execution of complex tasks in daily living. To examine the efficacy of these combined techniques, (i)ADL task performance will be evaluated using a standardized observation scale taking correct, ineffective and missing steps into account (Dechamps et al., 2007). The primary hypothesis is that combining errorless

![Figure 1](chart.png) Flowchart of the GMT algorithm and an example of its application.

<table>
<thead>
<tr>
<th>Stage 1</th>
<th>Stage 2</th>
<th>Stage 3</th>
<th>Stage 4</th>
<th>Stage 5</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Stop</strong></td>
<td><strong>Define</strong></td>
<td><strong>List</strong></td>
<td><strong>Learn</strong></td>
<td><strong>Check</strong></td>
</tr>
<tr>
<td>Stop</td>
<td>Define</td>
<td>List</td>
<td>Learn</td>
<td>Check</td>
</tr>
<tr>
<td>What am I doing?</td>
<td>The main task</td>
<td>The steps</td>
<td>The steps</td>
<td>Am I doing what I planned?</td>
</tr>
<tr>
<td>Do I know the steps?</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Do it</td>
<td>Check</td>
<td>Have I reached my goal?</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Example

What is my goal?

To process and organize my mail

1. Open the first envelope
2. Read the letter
3. Specify the category (e.g. bill, advertising)
4. Perform the corresponding action (e.g. pay the bill)
5. If necessary, file the letter
6. Open the next envelope
7. Repeat steps 2-6 for all letters

Have I reached my goal?
learning and GMT will result in a more efficacious intervention, when applied to (re)learning daily tasks in patients with executive disorders after acquired brain injury. This study may contribute to a better treatment of disorganized behaviour after brain injury and improve the cognitive rehabilitation of patients with executive disorders. From a patient perspective, it might consistently contribute to enhance the functional independence of brain-injured patients.

Methods

To evaluate the efficacy of GMT in which errorless learning is integrated, this approach will be compared with conventional GMT treatment in which an errorful approach is used. This comparison will be investigated in an assessor-blind randomized controlled trial that is registered at the Dutch Trial Register (No. NTR3567). The Medical Review Ethics Committee region Arnhem-Nijmegen approved the study (No. NL38019.091.11).

Participants and setting
The study population consists of brain-damaged patients referred for outpatient cognitive rehabilitation. Participants eligible for the study must have executive disorders due to acquired brain injury (ABI) of non-progressive nature (i.e., traumatic brain injury, stroke) in the chronic phase of the illness. Executive deficits will be assessed by an extensive neuropsychological examination.

Inclusion criteria
1. Non-progressive acquired brain injury;
2. Minimal post-onset time of 3 months;
3. Being in outpatient rehabilitation;
4. Having executive deficits, as established by neuropsychological examination;
5. Living independently at home;
6. Age: 18-70 years at onset.

Exclusion criteria
1. Inability to speak/understand the Dutch language;
2. Severe premorbid psychiatric problems;
3. Neurodegenerative disorders;
4. Substance abuse;
5. Severe cognitive comorbidity.

Setting
Patients will be recruited from the Rehabilitation Medical Centre Groot Klimmendaal in Arnhem, the Netherlands and the outpatient rehabilitation clinic for brain injured patients and the department of Neurorehabilitation of the Sint Maartenskliniek in Nijmegen, the Netherlands. In the course of 18 months 64 participants will be recruited.

Procedure
A flowchart of the study design is presented in Figure 2. An extensive neuropsychological assessment will be performed as part of the selection procedure. Participants are eligible for the study if they have executive impairments, objectified by neuropsychological examination. As executive functioning is a multifarious concept, the neuropsychological assessment is designed to cover five of its main aspects. To assess response generation (Lezak et al., 2012) the Category Fluency test (CFT) and the Letter Fluency test (LFT) will be administered. Planning will be measured with an altered version of the Modified Six Elements Test and the Zoo Map test (subtest of BADS; Wilson, Alderman, Burgess, Emslie, & Evans, 1996). The Go/No-go task from the computerized TAP 2.1 (Zimmermann & Fimm, 2007) will be used to examine response inhibition. Working memory will be assessed with Letter-Number Sequencing (LNS; subtest of the WAIS III; Wechsler, 1997) and task switching with the Brixton Spatial Anticipation test (Burgess & Shallice, 1997). Specifically, the criteria for having executive disorders and to be included in the study are either a standard score of 1.5 standard deviation (SD) below the normative mean on at least two of the seven executive tests or a standard score between 1 and 1.5 SD below the normative mean on at least four of those seven tests. Moreover, to obtain a complete cognitive profile of the participants, the Rivermead Behavioural Memory Test-Third Edition (RBMT III; Wilson et al., 2008) will be administered to assess episodic memory and the alertness subtest of the TAP 2.1 (Zimmermann & Fimm, 2007) will be used as a measure for attention and concentration. The National Adult Reading Test (NART; Dutch version) will be given to estimate premorbid IQ. All neuropsychological tests will be administered by a neuropsychologist or a trained assistant.

After fulfilling the inclusion criteria and obtaining the signed informed consents, participants will be randomly assigned to GMT with an errorless learning approach (experimental treatment) or to conventional GMT (treatment as usual) using trial and error learning.
Interventions

Both treatment arms will comprise eight one-hour individual sessions, administered twice a week by trained therapists. An overview of the content of the training sessions is shown in Table 1. Sessions 1-4 will take place at the participating centers. Sessions 5-8 will take place at the participants’ home or in the work environment, depending on the treatment goals. The first two sessions of GMT will be identical for both conditions. In the first session participants will be informed about GMT in general and about cognitive dysfunction, more specifically about executive dysfunction after acquired brain injury. In the second session each participant will choose two individual treatment goals. These treatment goals must be (i)ADL tasks and the participant has to experience difficulties performing the chosen tasks. Learning the correct execution of these (i)ADL tasks will be the main aim during the rest of the training sessions. Acceptable treatment goals are those which can be subdivided into multiple steps and should be defined in accordance with the SMART method (Specific, Measurable, Attainable, Reasonable, Timely) (Bovend’Eerdt, Botell, & Wade, 2009). After the second session a baseline assessment will take place. The execution of both treatment goals will be filmed, so that it can be evaluated later by assessors who are blind for allocation. After the baseline assessment participants will undergo training sessions 3-8 in the errorless learning condition or in the trial and error condition.

**GMT-Errorless learning condition**

The experimental treatment consists of GMT with an errorless learning approach, in which both the acquisition and application of GMT will be taught using error controlling methods. This implies active guidance from a therapist to prevent the occurrence of errors or guessing. Therefore, errorless learning techniques, such as verbal instructions, modeling and cue cards will be used, as well as written instructions of the chosen (i)ADL tasks. After the two tasks have been subdivided into multiple steps and have been rehearsed verbally during sessions 3 and 4, the actual execution of these steps is practiced in sessions 5 and 6 of the treatment. In these sessions cues will be faded after successful execution of the steps (i.e., without hesitation or errors). In sessions 7 and 8 the patient will be taught to check after each task step if the action was performed correctly and if it has led to the planned (subordinate) goals. ‘Checking’ is part of the final stage of the GMT algorithm and therefore both treatment goals will be fully integrated into the GMT algorithm and errorless execution of both complex tasks according to the GMT algorithm will be practiced.

**GMT-Trial and error learning condition**

In the conventional GMT errors are allowed to occur. Patients will learn to use the GMT algorithm and the performance of the tasks using trial and error learning. In this condition the therapist is not required to prevent errors during the application of the GMT strategy, but he/she only provides feedback in response to errors (i.e., afterwards). Also, therapists will not provide clues as how to solve problems and will not actively prompt or guide the execution of tasks. After having chosen two (i)ADL tasks in sessions 1 and 2, session 3 consists of a general description of the GMT algorithm by the therapist. In sessions 4 and 5 the participant is asked to define the task steps and complete the GMT schemes.

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**Figure 2** Flowchart of the study design.
for both treatment goals. The therapist will not help in defining the task steps and the main aim is to motivate the participant to complete the schemes. If errors occur, the therapist will not intervene, and the participant will have to detect these during the training. In sessions 6 and 7 the actual performance of the (i)ADL tasks will be practised, again using the above described trial and error approach. The participant will be motivated to actively practice performance and to seek solutions in the case of problems. Session 8 is again devoted to the execution of the tasks and to eventually improve the execution of task steps or the previous completed GMT schemes.

Objectives

The primary objective of this investigation is to examine the efficacy of a combined errorless learning and GMT intervention for the treatment of executive problems in patients with acquired brain injury (ABI). These patients are in the chronic phase of their illness and the study will focus on individually chosen complex daily tasks ((i)ADL), such as cleaning a bathroom, processing mail or preparing a meal. The hypothesis is that brain-injured patients will (re)learn performance of (i)ADL tasks more efficiently if an errorless learning method is used. That is, more task steps will be performed correctly and in the right sequence and less irrelevant and missing steps will be present. Consequently, more goals and sub goals will be attained by applying errorless learning in GMT.

Outcomes

An overview of the outcome measures is given in table 2. The main outcome will be (i)ADL task performance. Performance of each task step will be scored on a 3-point scale: 0) absence/incomplete: the task step is missing or incomplete; 1) questionable/ineffective: the task step is not correctly performed or not set in the correct sequence; 2) competent/correct: the task step is successfully performed and set in the correct sequence. Observed total scores will be converted into percentage scores to allow statistical comparison of data from different (i)ADL tasks, and comparison between groups. A similar scale was used in previous research (Dechamps et al., 2011) to assess (i)ADL task performance in patients with Alzheimer’s dementia. Task execution will be filmed and evaluation by using the scale will take place afterwards by an assessor who is not involved in the actual treatment to secure the blind nature of the design.

A secondary outcome measure will be goal attainment using Goal Attainment Scaling (GAS; Kiresuk & Sherman, 1968). GAS is an individualized method to evaluate the extent to which individual treatment goals are achieved by defining several levels of outcomes (as expected, (much) more than expected, (much)
less than expected). GAS is scored in a standardized way to allow statistical comparisons between individual treatment goals and is widely used in rehabilitation (Malec, 2009; Turner-Stokes, 2009). During session 2, GAS schemes for both treatment goals will be completed by the trainer in cooperation with the participant. During the post-treatment measurement, two GAS scores will be obtained, one by the patient and one by the trainer.

**Additional study parameters**

Questionnaires will be administered to measure several aspects of executive functioning. The Dysexecutive Questionnaire (DEX; Burgess, Alderman, Wilson, Evans, & Emslie, 1996), both the patient and the proxy version, will be used for the assessment of dysexecutive behaviour. Self-reported executive functioning will be measured using the Dutch version of the Executive Function Index (EFI-NL; Spinella, 2006). The Executive Observation Scale (EOS; based on Pollens, McBratnie, & Burton, 1988), completed by a proxy, will be used as an observation measure for executive function. The Cognitive Failures Questionnaire (CFQ; Broadbent, Cooper, Fitzgerald, & Parkes, 1982) will assess self-reported subjective cognitive complaints in general. Quality of life will be determined using the RAND 36-item Short Form Health Survey (RAND-36; Brazier et al., 1992).

**Baseline**

After the second session, in which two individual treatment goals ((i)ADL tasks) are established and the GAS schemes are completed by the trainer in cooperation with the participant, the baseline measurement will take place. During this assessment execution of both treatment goals will be filmed to secure the blind nature of the design. The recorded performance will be assessed by an independent research assistant using the standardized scale to guarantee blinding of condition.

**Post-treatment**

After treatment, (i)ADL task performance will be assessed again by filming and scoring task performance. The previous completed GAS schemes will be scored by participant and by trainer to evaluate goal attainment. The questionnaires and neuropsychological assessment, using parallel versions of the same tests, will be administered after treatment as well, to control for nonspecific recovery. The data gathered with the questionnaires and the neuropsychological tests provide measures for change in insight, executive complaints, subjective and objective executive functioning for moderator analyses, to examine possible determinants for treatment success.

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Recruitment- and outcome variables.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Outcome measure</td>
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<td>Quality of Life</td>
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Sample size
Determination of the sample size for this study is based on data from a RCT examining the effects of a structured 6-week Goal Management Training (Van Hooren et al., 2007). In each group, 32 participants are required to detect an effect size of $d=0.6$ with a power=.80 and $\alpha=.05$. These estimated sample sizes are comparable with other studies evaluating the efficacy of different types of GMT (Van Hooren et al., 2007; Spikman, Boelen, Lamberts, Brouwer, & Fasotti, 2010).

Randomization and blinding
Allocation of participants to either condition will be established using a computer generated block randomization procedure (block size n=4) without stratification. The written information to inform patients about the study only mentions that two types of GMT will be compared. To achieve participant blinding, no information will be given about specific differences between the two conditions. Assessor blinding will be achieved by filming the (i)ADL task performance of the participants. All hints of treatment condition will be avoided and performance will be scored by research assistants who are not involved in delivering GMT.

Statistical analysis
All data will be analyzed with IBM SPSS 19. The normality of all variables will be checked and corrected for, if necessary. The performance on the neuropsychological tests will be compared with normative data and corrected for age and education. Descriptive statistics of relevant variables will be obtained and compared for the two treatment arms using analysis of variance.

To evaluate the efficacy of GMT-errorless learning compared to conventional GMT with trial and error learning, pre- and post training data will be analyzed using a 2x2 repeated measure analysis of variance (General Linear Model) with treatment condition (GMT-errorless learning and conventional GMT) as between-subject factor and measurement (pre- and post-treatment) as within-subject factor. The dependent variable will be the standardized scale score (quantitative). The same analysis will be done for the secondary outcome measure, the GAS scores. Appropriate post-hoc tests will be performed and effect sizes (partial eta-squared) will be computed. Moreover, correlations will be computed between moderator variables (questionnaires and neuropsychological tests) and treatment effects (difference score: post treatment minus baseline).

The background variables of the participants in both treatment conditions are expected to be comparable (age, education level, estimation IQ) because of the randomization procedure. In case of significant differences, appropriate statistical adjustment for confounding variables will be performed (ANCOVA). All statistical tests will be two-tailed, alpha set at 0.05.

Discussion
Both Goal Management Training and errorless learning are two methods that have been separately well studied and shown to be effective. Up to now however, the two methods have never been combined. Combining an errorless learning approach with GMT is expected to optimize the acquisition of the GMT algorithm and to improve the performance of complex daily tasks in brain-injured patients with executive deficits. Consequently, the efficacy of the intervention is increased, which may contribute to functional independence of patients with acquired brain injury. Not only does the combination of methods provide an evidence-based intervention for clinical practice, the present study may also contribute to more insight into the underlying mechanisms of errorless learning. Previous studies investigating errorless learning have often focused on patients with profound memory impairments, such as patients with Alzheimer’s disease or Korsakoff’s syndrome (Clare & Jones, 2008; Kessels & De Haan, 2003). The assumption was that due to a dysfunctional explicit memory system errors were not consciously corrected and implicitly consolidated (Kessels & Olde Hensken, 2009). However, the beneficial effects of errorless learning may also be related to a failing error monitoring system. That is, the inability of patients with executive dysfunction to detect errors (Bettcher et al., 2008). The current study proposal focuses on patients with primarily executive impairments in whom the presence of memory impairments is less prominent. This suggests that explicit memory is relatively spared in these patients, whereas their error-monitoring system is failing. As a result, the current study may contribute to a better understanding of these two underlying mechanisms of errorless learning.

Previous studies investigated GMT used paper-and-pencil tasks or fixed (i)ADL tasks, such as meal preparation (Levine et al., 2000) and financial management (Grant et al., 2012). A strength of this study is that participants will choose their own individual (i)ADL tasks that will be (re)learned during the training. Individual goals correspond to individual lifestyles and demands and may therefore provide a more fitting contribution to daily functioning and enhance functional independence of the participants.

In summary, the aim of the study is to examine the efficacy of Goal Management Training combined with an errorless learning approach as a treatment of executive problems in patients with acquired brain injury in the chronic phase, focusing on execution of complex daily-life tasks. This study could contribute to a better treatment of executive deficits in cognitive rehabilitation.
Five A randomized controlled trial of errorless Goal Management Training in persons with brain injury

Published as:
Abstract

Both errorless learning (EL) and Goal Management Training (GMT) have been shown effective cognitive rehabilitation methods aimed at optimizing the performance on everyday skills after brain injury. We examined whether a combination of EL and GMT is superior to traditional GMT for training complex daily tasks in brain-injured patients with executive dysfunction. This assessor-blinded randomized controlled trial was conducted in 67 patients with executive impairments due to brain injury of non-progressive nature (minimal post-onset time: 3 months), referred for outpatient rehabilitation. Individually selected everyday tasks were trained using 8 sessions of an experimental combination of EL and GMT, which follows a trial-and-error approach. Primary outcome measure was everyday task performance assessed after treatment compared to baseline. Goal attainment scaling, rated by both trainers and patients, was used as secondary outcome measure.

Errorless GMT improved everyday task performance significantly more than conventional GMT (adjusted difference 15.43, 95% confidence interval [CI] 4.52 to 26.35; Cohen’s d=0.74). Goal attainment, as scored by the trainers, was significantly higher after EL-GMT compared to conventional GMT (mean difference 7.34, 95% CI 2.99 to 11.68; Cohen’s d=0.87). The patients’ goal attainment scores did not differ between the two treatment arms (mean difference 3.51, 95% CI -1.41 to 8.44). Our study is the first to show that preventing the occurrence of errors during executive strategy training enhances the acquisition of everyday activities. The experimental errorless GMT intervention is a valuable contribution to cognitive rehabilitation in clinical practice.

Introduction

Executive deficits are prominent and persistent cognitive impairments after brain injury, which are often the result of frontal lobe or posterior-subcortical damage. These deficits include impairments in planning, self-monitoring and goal-directed behavior (Cicerone, Levin, Malec, Stuss, & Whyte, 2006; Hart & Evans, 2006; Stuss, 2011). Even subtle executive deficits can provoke difficulties in learning and performing daily life activities, hampering quality of life (Boelen, Spikman, Rietveld, & Fasotti, 2009). Therefore, the development of rehabilitation interventions focusing on executive dysfunction is warranted. One of these interventions is Goal Management Training, which entails learning and applying an algorithm that subdivides complex tasks into multiple task steps (Robertson, 1996). During Goal Management Training patients are prompted to keep both the final goal and the task steps active in working memory, and to monitor their behavior and intentions during the execution of each task step.

Several studies have shown that Goal Management Training contributes to a better performance on everyday tasks in brain-injured patients. Levine et al. (2006) were the first to examine its effects in a randomized controlled trial in which Goal Management Training was compared to motor skills training in thirty patients with traumatic brain injury. Only Goal Management Training resulted in significant improvements on everyday paper-and-pencil tasks, such as proofreading a short text or grouping columns of words into categories. Moreover, they reported improvement in meal-preparation abilities in a patient with encephalitis after application of Goal Management Training. More recently, Grant, Ponsford and Bennett (2012) investigated the efficacy of Goal Management Training on day-to-day financial management using a multiple-case design. Three of the four brain-injured participants who completed the training fulfilled or even exceeded their a priori predicted levels of goal attainment. Other studies that applied Goal Management Training in larger groups of patients with acquired brain injury combined it with other cognitive rehabilitation methods. For example, auditory cueing was integrated into Goal Management Training (Fish et al., 2007; Manly, Hawkins, Evans, Woldt, & Robertson, 2002). Others (Miotto, Evans, De Lucia, & Scaf, 2009; Spikman, Boelen, Lamberts, Brouwer, & Fasotti, 2010) combined Goal Management Training with problem solving therapy.

In addition to Goal Management Training, another well-investigated method for training everyday tasks is errorless learning. Here, the occurrence of errors during the learning process is prevented in contrast to ‘normal’ trial-and-error learning, in which errors may occur naturally (Baddeley, 1992). Previous studies have shown that an errorless learning approach in patients with memory impairments improves task performance compared to trial-and-error learning.
In contrast, persons without cognitive deficits reap the benefits of committed learning. Therefore, amnesic patients may easily confuse correct and erroneous information previously encountered.

Frontal areas are also involved in planning and performing executive multistep tasks. It is well known, that while planning and carrying out these multistep tasks, patients with executive problems already overcharge their executive processing system, resulting in so-called ‘goal-neglect’ (Duncan, 1986). Concurrently monitoring and correcting errors (i.e., error monitoring) during task execution increases the demands on this already vulnerable executive system. Therefore, errors might be confused with correct actions and stored accordingly. Hence, errorless learning may also be beneficial for executively impaired patients. However, little research has been performed investigating the benefits of errorless learning in executively impaired patients (Clare & Jones, 2008). Cohen, Ylvisaker, Hamilton, Kemp, and Claiman (2010) used errorless learning in a single patient with both memory and executive deficits. Here, several everyday domains were trained, including communication in social situations (e.g., selecting appropriate conversation topics using cue cards), prospective memory (e.g., remember to bring items when leaving home) and activities in daily living (for example, completing budget sheets and performing banking transactions). Results showed an improvement in everyday tasks as well as beneficial effects on the patients’ quality of life. In addition, Pitel et al. (2006) used errorless learning in two patients with memory and executive deficits, and showed that this approach was effective in teaching these patients complex semantic information. These limited findings stress the need to further investigate errorless learning in dysexecutive patients.

Patients with executive dysfunction typically display problems in both strategic behavior and outcome monitoring, which includes the inability to identify and keep track of their own errors. Therefore, a combination of Goal Management Training and errorless learning may be beneficial. That is, errorless learning may overcome impaired outcome monitoring which is essential for successful application of the Goal Management Training algorithm. As a result, preventing the occurrence of errors may optimize the outcome of Goal Management Training in patients with executive dysfunction. In the present multicenter single-blinded randomized controlled trial, both the Goal Management Training strategy and its application in individually selected everyday tasks (i.e., treatment goals) were taught using error reducing methods. That is, the algorithm itself was presented using a stepwise approach and the treatment goals were practised in accordance with the principles of errorless learning. We hypothesize that a combined errorless learning and Goal Management Training is more effective than conventional Goal Management Training in brain-injured patients with executive deficits.

**Methods**

**Participants**

Brain-injured patients referred for outpatient cognitive rehabilitation were recruited between 2012 and 2014. To be eligible for inclusion, participants had to have executive impairments due to an acquired brain injury of non-progressive nature (e.g., traumatic brain injury or stroke). They had to be in the chronic stage (minimal post-onset time of three months). Executive impairments were assessed with a comprehensive neuropsychological testing, including seven executive function tests. Test inclusion criteria were (a) a standard score of 1.5 SD below the normative mean on at least two out of the seven executive function tests or (b) a standard score between 1 and 1.5 SD below the normative mean on at least four of these tests or (c) a standard score of 1.5 SD below the normative mean on one executive function test and a standard score between 1 and 1.5 SD below the normative mean on at least 2 of the remaining executive function tests. Age of the participants had to be between 18 and 70 years at onset and they had to live independently at home. Patients were excluded if they were unable to understand or speak Dutch (for the participants in the Netherlands) or Italian (for the participants in Italy), had severe non-executive comorbidity (such as amnestic syndrome, neglect or aphasia), or a history of neurodegenerative disease or psychiatric disorder. Based on previous research examining the effects of a structured 6-week Goal Management Training on cognitive failures (Van...
Hooren et al., 2007), a sample size of 32 participants in each group was required to detect an effect size of 0.6 with a power of 0.80 and alpha set at 0.05. This estimated sample size is comparable with other studies evaluating the efficacy of different types of Goal Management Training (e.g., Van Hooren et al., 2007; Spikman et al., 2010).

Procedure
A detailed description of the study rationale and protocol is described in Bertens, Fasotti, Boelen, and Kessels (2013). Four rehabilitation institutions participated in the study: Rehabilitation Medical Centre Groot Klimmendaal (Arnhem, the Netherlands), Sint Maartenskliniek (Nijmegen, the Netherlands), Centro Polifunzionale Don Calabria (Verona, Italy) and Associazione Trauma Cranico Daccapo, (Padua, Italy). The study is registered at the Netherlands Clinical Trials Registry (reference no. NTR2367) and approved by the Medical Review Ethics Committee region Arnhem-Nijmegen (reference NL38019.091.11). Participants gave written informed consent before taking part in the study and all data was obtained in compliance with the Helsinki Declaration. The trial is reported in accordance with the CONSORT guidelines (Schulz, Altman, & Moher, 2010).

The psychologists of the participating centers identified potential participants and the neuropsychological test battery was administered to assess executive impairments. Randomization was performed by the first author using a computerized block randomization procedure with a block size of 4 by generating a random number list using Random Allocation Software (RAS; http://randomallocatio.sourceforge.net/). The allocation was performed in the order of recruitment using the aforementioned randomly generated sequences. Patients were blind for treatment condition and were only told that two variants of Goal Management Training strategy were taught using error reducing methods. The experimental treatment consisted of Goal Management Training with an errorless learning approach, that is, both the acquisition and application of the errorless (errorless) and the conventional Goal Management Training comprised of 8 one-hour individual sessions, administered twice a week by trainers. These trainers were occupational therapists (N = 4) and psychologists (N = 7) with a background in neuropsychology. To warrant treatment fidelity, all sessions of both treatments were described in detail in the corresponding protocols. Each trainer followed a 4-5 hours practice session led by the main researcher before engaging in patient-related activities. Moreover, the first 4 sessions (and more, if deemed necessary) were given by the main researcher and the trainer in conjunction to ensure protocol adherence. The main researcher could always be contacted when necessary. All trainers taught patients in both conditions. Sessions 1-4 took place in the participating centers, whereas sessions 5-8 took place at the participants’ home or in the participants’ work environment, depending on the selected treatment goals. The first two sessions were identical in both treatment arms. In the first session, patients were informed about cognitive and executive impairments after brain injury. Moreover, the participants were given several questionnaires and were asked to complete and return these questionnaires at the start of the second session. During the second session two individual treatment goals were established. These goals were chosen by the patient in cooperation with the trainer. For both goals, Goal Attainment Scaling schemes (i.e., defining potential levels of outcome) were completed by the trainer, also in cooperation with the participant.

Experimental intervention
The experimental treatment consisted of Goal Management Training with an errorless learning approach, that is, both the acquisition and application of the Goal Management Training strategy were taught using error reducing methods. This implies active guidance from a trainer to prevent the occurrence of errors or guessing. Therefore, errorless learning techniques, including verbal and written instructions, cue cards and modeling were used. The occurrence of errors during the individual training sessions was not rated, but errors were reduced to a minimum by these error-prevention strategies. During sessions 3 and 4 (hence the first two sessions of this treatment arm) the two previously selected everyday tasks were subdivided into multiple task steps and written down in schemes which were rehearsed verbally. Care was taken that these schemes did not include any erroneous or ambiguous steps. These steps were practised in sessions 5 and 6. In these sessions instructions and cues were faded after successful performance of the steps (without hesitation or errors). After each task step in sessions 7 and 8, the patient was taught to check whether the steps and the final goal. If not, the patient has to restart the entire algorithm from stage 1 (Levine et al., 2000). In the present study, both the experimental (errorless) and the conventional Goal Management Training comprised of 8 one-hour individual sessions, administered twice a week by trainers. These trainers were occupational therapists (N = 4) and psychologists (N = 7) with a background in neuropsychology. To warrant treatment fidelity, all sessions of both treatments were described in detail in the corresponding protocols. Each trainer followed a 4-5 hours practice session led by the main researcher before engaging in patient-related activities. Moreover, the first 4 sessions (and more, if deemed necessary) were given by the main researcher and the trainer in conjunction to ensure protocol adherence. The main researcher could always be contacted when necessary. All trainers taught patients in both conditions. Sessions 1-4 took place in the participating centers, whereas sessions 5-8 took place at the participants’ home or in the participants’ work environment, depending on the selected treatment goals. The first two sessions were identical in both treatment arms. In the first session, patients were informed about cognitive and executive impairments after brain injury. Moreover, the participants were given several questionnaires and were asked to complete and return these questionnaires at the start of the second session. During the second session two individual treatment goals were established. These goals were chosen by the patient in cooperation with the trainer. For both goals, Goal Attainment Scaling schemes (i.e., defining potential levels of outcome) were completed by the trainer, also in cooperation with the participant.
action was performed correctly and whether it resulted in the planned (subordinate) goals. ‘Checking’ of the task steps is a crucial part of the final stage of the Goal Management Training algorithm. Consequently, both treatment goals were errorlessly taught and fully integrated into the Goal Management Training strategy.

Control intervention
In the conventional Goal Management Training errors were allowed to occur. Patients were taught to apply the Goal Management Training algorithm to the execution of the tasks using trial-and-error learning. In this condition the trainer did not prevent errors during the acquisition and the application of the Goal Management Training strategy; but provided feedback afterwards, that is, in response to errors. Also, trainers neither assisted the patients in solving problems, nor actively prompted or guided the task performance. As a consequence, errors occurred frequently, but these were not rated during the individual learning sessions. After having selected two activities of daily living (i.e., the treatment goals) in sessions 1 and 2, the trainer described the Goal Management Training algorithm in session 3 in general terms. Subsequently, the participant was asked to define and write down the task steps of both treatment goals in Goal Management Training schemes during sessions 4 and 5. The trainer did not assist in defining the task steps, but encouraged the participant to complete the schemes. If a participant made any errors, the trainer did not intervene, as the participants themselves had to detect and correct these during the training. The selected everyday activities were actually practised in sessions 6 and 7, again using a trial-and-error approach. The trainer motivated the participant to actively perform the activity and to solve any problems that occurred during the task performance. Finally, task performance could be further optimized in session 8 using the previously completed Goal Management Training schemes.

Outcome Measures
Everyday task performance
The primary outcome was task performance of the trained tasks, as rated by assessors who were blinded for treatment arm. Execution of these tasks was filmed twice, once at baseline (after the second session) and once after training (after the eighth session). These films were used to rate the performance using a standardized rating based on a method developed by Dechamps et al. (2011). Assessors subdivided each task into individual task steps. Subsequently, performance of each task step was scored on a 3-point rating scale: 0) stood for an absent/incomplete step; 1) meant a questionable/ineffective step; such a task step was not correctly performed or not carried out in correct order; 2) denoted a competent/correct step, that is, a step that was successfully performed and achieved in the correct sequence. The raw ratings were converted into percentage scores to allow statistical comparison of data from different activities of daily living. For each participant the two percentage treatment goals were averaged to obtain one everyday task performance score per participant, both at baseline and after treatment.

Goal attainment scaling
A secondary outcome measure was goal attainment scaling, used to quantify the extent to which treatment goals were achieved (Bovend’Eerdt, Botell, & Wade, 2009; Kiresuk & Sherman, 1968). Goal attainment scaling enables to evaluate individual goals in a standardized way, using predefined levels of achievement based on current and expected performance (Turner-Stokes, 2009) and is frequently used in rehabilitation research. A 6-point Goal Attainment Scale (Steenbeek, Meester-Delver, Becher, & Lankhorst, 2005) was used, in which level 0 represents the expected level of achievement and -2 describes the baseline level. Level -1 represents partial achievement, -3 represents a worsening of achievement level, and +1 and +2 respectively indicate small and remarkably better than expected levels of achievement. Goal Attainment Scale schemes (i.e., defining the 6 possible levels of achievement) for both treatment goals were completed by the trainer in cooperation with the participant during the second session. After the intervention, both the patient and trainer indicated the achieved level, resulting in separate patient and trainer Goal Attainment Scale scores.

Moreover, a comprehensive neuropsychological assessment, with a duration of approximately 90 minutes and consisting of Dutch and Italian (for the Dutch and Italian participants respectively) versions of widely used and well-validated tests, was administered to determine the eligibility of the recruited patients and to obtain a cognitive profile of the participants. The main aspects of executive functioning were assessed using Verbal Fluency tests (category and letter fluency; Schmand, Groenink, & Van den Dungen, 2008) for response generation, a Modified Six Elements Test (MSET; Bertens, Frankenmolen, Boelen, Kessels, & Fasotti, 2015) and the Zoo Map Test (subtest of the Behavioural Assessment of the Dysexecutive Syndrome; Wilson, Alderman, Burgess, Emslie, & Evans, 1996) measuring planning, Letter-Number Sequencing (LNS) (subtest of the Wechsler Adult Intelligence Scale – Third Edition; Wechsler, 1997) to assess working memory, the Go/No-Go subtest from the Test for Attentional Performance (TAP 2.1; Zimmermann & Fimm, 2007) to measure inhibition and the Brixton Spatial Anticipation test (Burgess & Shallice, 1997) to assess concept shifting. In addition,
memory was assessed using the Rivermead Behavioural Memory Test; the RBMT-3 (Wilson et al., 2008) was used for the Dutch participants and the RBMT (Wilson, Cockburn, Baddeley, & Hiorns, 1989) for the Italian participants. The Alertness subtest of the TAP 2.1 (Zimmermann & Fimm, 2007) was administered to assess attention and concentration. For the neuropsychological test variables raw scores were reported in accordance with the test’s manuals. The National Adult Reading Test (NART; Nelson & O’Connell, 1978) was used to estimate premorbid IQ, that is the Dutch (Schmand, Lindeboom, & Harskamp, 1992) and Italian (Sartori, Colombo, Vallar, Rusconi & Pinarello, 1995) versions for the Dutch and Italian participants respectively.

Several questionnaires were administered to assess subjective cognitive function. Self-reported executive functioning was assessed using the Executive Function Index (EFI; Spinella, 2005), cognitive complaints were measured by the Cognitive Failures Questionnaire (CFQ; Broadbent, Cooper, FitzGerald, & Parkes, 1982), dysexecutive behavior was assessed with the Dysexecutive Questionnaire (DEX; Wilson et al., 1996) completed by the patient and a proxy separately, and quality of life was assessed using the RAND 36-item Short Form Health Survey (RAND-36; Brazier et al., 1992). These questionnaires were completed after the first session.

Statistical Analysis
Possible demographic differences between the groups at baseline were investigated using t-tests or nonparametric tests for nominal or ordinal variables (sex distribution, type of brain injury, and time since injury). In addition, we conducted an analysis of covariance on the primary outcome measure, the video performance ratings. To adjust for baseline differences, the post treatment scores of the errorless learning Goal Management Training and the conventional Goal Management Training groups were evaluated with video rating baseline scores and, when applicable, demographic differences as covariate(s). Changes between baseline and post-treatment for the groups separately were analyzed using paired samples t-tests. The adjusted effect size (Cohen’s d) was calculated by dividing the adjusted treatment effect (i.e., adjusted mean errorless learning Goal Management Training minus adjusted mean conventional Goal Management Training) by the residual standard deviation (i.e., the adjusted root mean square error; cf. Graff et al., 2006). We also computed the proportion of patients who achieved a clinically significant improvement, that is, an improvement of at least two standard deviations from the baseline mean (Evans, Margison, Barkham, 1998; Jacobson & Truax, 1991). We analyzed the Goal Attainment Scale scores by converting the raw scores for both goals of each patient into one T-score (Kiresuk & Sherman, 1968; Turner-Stokes & Williams, 2010). T-scores of the patients and those of the trainers were analyzed separately. Because baseline Goal Attainment Scale scores were equal for all patients, only post treatment (achieved) Goal Attainment Scale scores were compared using t-tests. Here, effect sizes were calculated using Cohen’s d. We conducted paired samples t-tests to evaluate the difference between baseline and post-treatment for each treatment arm. For the statistical analyses IBM SPSS 20.0 was used and alpha was set at 0.05 for all analyses.

Results
A total of 205 patients were tested to evaluate executive functioning and eligibility. Of these, 79 patients fulfilled the inclusion criteria of whom 12 patients refused to participate (unable to undergo treatment twice a week, or not interested in participating in a study). Three patients in the errorless learning Goal Management Training and four in the conventional group did not complete the treatment because no treatment goals could be established. The remaining 60 patients all completed the training with 30 patients in the experimental errorless learning Goal Management Training and 30 in the conventional Goal Management Training. The CONSORT diagram (Figure 1) shows the flow of the participants through the trial. Table 1 shows the demographic characteristics and the baseline performance on the neuropsychological tests and questionnaires for both groups. Demographic features (age, sex distribution, estimated IQ and years of education) and type and duration of brain injury did not differ between the two groups. Furthermore, there were neither differences in cognitive functioning as measured by the neuropsychological tests, nor in cognitive complaints and quality of life as reported by the participants and proxies using the questionnaires.

Table 2 presents a categorical overview and examples of the selected treatment goals (categories in accordance with Vlagsma et al., in press). The treatment goals covered the main aspects of daily living. Most treatment goals were related to housekeeping (including gardening) (28%), usually cleaning a space or room, followed by financial and administrative goals (23%) such as conducting an online banking transaction, and goals concerning the management of leisure time (19%) like planning a day trip. Remaining goals were related to mobility (8%; e.g., route planning) and communication (8%; e.g., sending an email).
Table 1 Continued.

<table>
<thead>
<tr>
<th>Demographic characteristic</th>
<th>Errorless learning Goal Management Training</th>
<th>Conventional Goal Management Training</th>
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<tr>
<td>Etiology</td>
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<tr>
<td>Traumatic brain injury</td>
<td>53% 16</td>
<td>33% 10</td>
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<tr>
<td>Stroke</td>
<td>43% 13</td>
<td>63% 19</td>
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<tr>
<td>Other</td>
<td>3% 1</td>
<td>3% 1</td>
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<tr>
<td>Localization</td>
<td></td>
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<tr>
<td>Supratentorial</td>
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<td>Bilateral / diffuse</td>
<td>57% 17</td>
<td>50% 15</td>
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<tr>
<td>Unilateral</td>
<td>40% 12</td>
<td>47% 14</td>
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<tr>
<td>Brainstem</td>
<td>3% 1</td>
<td>0% 0</td>
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<tr>
<td>Cerebellum</td>
<td>0% 0</td>
<td>3% 1</td>
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<td>Neuropsychological tests</td>
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<tr>
<td>Category fluency</td>
<td>31.4 7.2 29</td>
<td>31.4 10.3 30</td>
<td>.98</td>
</tr>
<tr>
<td>Letter fluency</td>
<td>26.3 8.6 30</td>
<td>27.4 10.0 29</td>
<td>.66</td>
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<tr>
<td>Go/No-Go (TAP 2.1)</td>
<td>676.4 93.3 30</td>
<td>650.1 124.9 30</td>
<td>.36</td>
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<td>Modified Six Elements Test</td>
<td>4.0 1.8 30</td>
<td>4.5 1.6 30</td>
<td>.25</td>
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<td>Zoo Map (BADS)</td>
<td>5.5 4.6 30</td>
<td>7.8 5.1 29</td>
<td>.08</td>
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<tr>
<td>Letter-Number Sequencing</td>
<td>7.6 3.1 30</td>
<td>8.8 3.1 30</td>
<td>.14</td>
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<td>Brixton Spatial Anticipation Test</td>
<td>35.0 7.2 28</td>
<td>37.1 8.1 30</td>
<td>.31</td>
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<tr>
<td>RBMT</td>
<td>51.3 10.5 6</td>
<td>46.5 2.9 6</td>
<td>.32</td>
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<td>RBMT-3</td>
<td>116.3 19.8 23</td>
<td>123.7 19.1 22</td>
<td>.21</td>
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<tr>
<td>Alertness (TAP 2.1)</td>
<td>365.6 170.1 29</td>
<td>348.2 210.2 28</td>
<td>.73</td>
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<td>Questionnaires</td>
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<tr>
<td>Cognitive Failures Questionnaire</td>
<td>87.1 14.4 29</td>
<td>82.4 15.4 29</td>
<td>.29</td>
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<tr>
<td>Dysexecutive Questionnaire</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Patient</td>
<td>27.6 11.2 29</td>
<td>27.9 11.5 30</td>
<td>.92</td>
</tr>
<tr>
<td>Proxy</td>
<td>30.0 11.5 28</td>
<td>28.5 13.0 29</td>
<td>.65</td>
</tr>
<tr>
<td>Executive Function Index</td>
<td>95.9 9.4 27</td>
<td>91.5 9.8 29</td>
<td>.09</td>
</tr>
<tr>
<td>RAND-36</td>
<td>106.1 16.1 28</td>
<td>103.9 16.4 28</td>
<td>.61</td>
</tr>
</tbody>
</table>

Notes: TAP = Test for Attentional Performance; BADS = Behavioural Assessment of the Dysexecutive Syndrome; RBMT = Rivermead Behavioural Memory Test; RAND-36– RAND 36-item Short Form Health Survey.* Brain tumor (resection) * autoimmune encephalitis.
with a mean difference of 34.65 (95% CI 25.81 to 43.50; t(29) = 8.02, p < .001) for the errorless learning Goal Management Training group and a mean difference of 16.96 (95% CI 9.93 to 24.00; t(29) = 4.93, p < .001) for the conventional Goal Management Training group. Overall, 43% of the patients who received the combined errorless learning and Goal Management Training and 13% of the patients who received the conventional training achieved a clinically significant improvement.

**Goal attainment scaling**

Compared to baseline both the trainers and the patients reported significantly higher post treatment goal attainment scores in both treatment arms. For the errorless learning Goal Management Training the mean differences were 22.01 (95% CI 18.65 to 25.37; t(29) = 13.39, p < .001) for the trainer scores and 25.11 (95% CI 21.43 to 28.79; t(29) = 13.97 , p < .001) for the patient scores. For the conventional Goal Management Training the mean differences were 14.67 (95% CI 11.77 to 17.57).

**Outcome Variables**

**Everyday task performance**

Figure 2 shows the results of the performance on the primary outcome variable (everyday task performance as measured by the video performance ratings) at baseline and post training. Both the errorless learning and the conventional Goal Management Training group performed better on everyday tasks after training compared to baseline. The errorless learning Goal Management Training group (M = 69.13, SD = 23.59) performed significantly better on activities of daily living than the conventional Goal Management Training group (M = 58.63, SD = 25.01) after adjusting for the performance at baseline (M = 34.48, SD = 18.99 for the errorless learning Goal Management Training group; M = 41.67, SD = 18.93 for the conventional Goal Management Training group), F (1,57) = 8.02, p = .006, with a higher adjusted difference in performance of 15.43 (95% CI 4.52 to 26.35). Cohen's effect size value (d = 0.74) indicates a moderate to large effect. Paired sample t-tests showed that both groups improved significantly
Brain-injured patients with executive impairments perform better in everyday executive tasks when these have been learned with a combination of errorless learning and Goal Management Training instead of Goal Management Training alone. Both video performance rating scores from independent assessors and goal attainment scores obtained from trainers indicate that errorless Goal Management Training is superior to conventional Goal Management Training. Goal attainment as reported by the participating patients did not show a difference between the two learning methods. This apparent contrast between the patient and the trainer goal attainment scores may be explained by the patients’ lack of insight (Schiehser et al., 2011; Sherer et al., 1998) that may have led them to overestimate their levels of everyday functioning. Their relatively high goal attainment scores in both treatment arms support this explanation.

The trainers, who were not blind for treatment condition, may have been biased in scoring the extent of goal achievement. This may have resulted in an overly positive view of the combined errorless learning and Goal Management Training and may also explain the discrepancy with the ratings by the patients themselves. A recent systematic review (Krasny-Pacini, Chevignard, & Evans, 2014) identified 12 studies that investigated the efficacy of Goal Management Training in patients with acquired brain injury. This review argued that Goal Management Training was most effective when it was combined with other intervention methods. Moreover, the authors of the review recommended to use patients’ individual selected goals including everyday tasks, plan more than one training session per week with a total training duration of at least 15 sessions and to use external cues or prompts, such as periodically content-free auditory alerts (‘bleeps’; Manly, Hawkins, Evans, Woldt, & Robertson, 2002) to remind the participants to apply the Goal Management Training strategy. In our study external cueing was given by using errorless learning techniques such as verbal and visual instructions (e.g., cue cards) used for learning the task steps and the application of the Goal Management Training strategy (i.e., prompting to include ‘checking moments’ after execution of each task step and reminding to keep the overall goal actively in mind).

Although the efficacy of errorless learning has traditionally been investigated in laboratory tasks, various recent studies have examined the effects of errorless learning on the performance of everyday tasks. These studies, however, have mainly focused on amnesic patients, such as patients with Alzheimer’s dementia or Korsakoff’s syndrome (see De Werd, Boelen, Olde Rikkert, & Kessels, 2013; Middleton & Schwartz, 2012, for critical reviews) Our study is the first to combine Goal Management Training and errorless learning to investigate the

![Figure 3](image-url)
previously hypothesized benefits (Clare & Jones, 2008) of errorless learning for training everyday task performance, specifically in executively impaired patients.

In contrast to earlier studies that investigated the effects of Goal Management Training on one or two predefined daily tasks (Levine et al., 2000; Grant, Ponsford & Bennett, 2012; Fish et al., 2007) or on questionnaires and standardized tests (Manly et al., 2002; Miotto et al., 2009), the current study had a tailored approach by using everyday tasks selected by the patients. By using the current rating method and calculating percentage scores, the performance on a variety of tasks could be compared, which made it possible to evaluate the eligibility of the experimental treatment for training a broad spectrum of everyday tasks. The individually chosen treatment goals may also have contributed to the motivation of the participants, as all participants completed the training once treatment goals were established.

Previous studies have shown that Goal Management Training is an effective training method for persons with executive problems. Therefore, we did not include a condition in which participants simply practised the selected tasks (i.e., without the Goal Management Training strategy). As a result, our approach did not allow an assessment of the efficacy of Goal Management Training as such, in addition to the effects of repeated task practice. Future trials should therefore include more treatment arms, including a ‘task-practice only’ group and an ‘errorless learning only’ group.

Pinpointing treatment goals was not feasible in seven patients, possibly due to lack of awareness as a consequence of their executive deficits. However, this may also have been due to several other factors, such as motivational problems, avoidance behavior or fear of failure. Another limitation of our study was that it was not possible to blind the trainers to treatment condition. As a result, rater bias cannot be ruled out with respect to the Goal Attainment Scale scores of the trainers. Moreover, the trainers were instructed in how to employ the treatment protocols and gave several sessions in conjunction with the main researcher before delivering the training independently. However, treatment integrity was not systematically monitored, which is also a limitation. Furthermore, the examined intervention was task-specific and transfer to untrained tasks may hence not be expected. However, one could also argue that if the Goal Management Training algorithm was successfully acquired using an errorless approach, it may also be applied in non-trained tasks. Transfer effects could not be studied using the present setup, but future studies could also investigate whether untrained tasks benefit from an errorlessly acquired goal management strategy. For now, the application of errorless Goal Management Training must focus on tasks that are functionally important to the individual. In addition, no follow-up measurements were included. Therefore, the maintenance of the treatment effect is unknown, which should be investigated in future research.

In conclusion, our study is the first to show that combining errorless learning with Goal Management Training improves everyday tasks performance in brain-injured patients with executive impairments. Old errors do not always lead to new truths in executively impaired patients due to an inadequate monitoring of errors and behavior. Avoiding errors during the acquisition of daily activities circumvents a dysfunctional error-monitoring system and consequently prevents the implicit consolidation of errors in memory. Executive impairments after brain injury may have a devastating impact on everyday life (Burgess & Simons, 2005; Dawson, Binns, Hunt, Lemsny, & Polatajko, 2013) and compromise functional independence (Levine et al., 2000). Consequently, training individually selected daily tasks contributes to a more independent functioning of brain-injured patients and thus may decrease the amount of assistance needed at home or in vocational settings. The combination of errorless learning and Goal Management Training is a valuable contribution to cognitive rehabilitation in clinical practice.
Six Transfer effects of Errorless Goal Management Training on cognitive function and quality of life in brain-injured individuals

Submitted for publication as:
Abstract

Combining errorless learning and Goal Management Training (errorless GMT) has been shown effective in enhancing everyday task performance in brain-injured persons. In this brief report, we examined additional effects of errorless Goal Management Training (GMT) on cognitive function and quality of life after acquired brain injury. Sixty-seven patients with executive impairments after non-progressive acquired brain injury (>3 months post-injury), referred for outpatient rehabilitation, were randomly allocated to an experimental Errorless Goal Management Training (n=33) or conventional Goal Management Training (n=34). The aim was to train two individually chosen everyday tasks. In the errorless Goal Management Training, the occurrence of errors was prevented during learning, whereas, standard trial-and-error learning was applied in conventional Goal Management Training. Before and after training, objective cognitive function was assessed using neuropsychological tests, and subjective cognitive complaints and quality of life were evaluated using questionnaires. No significant interaction effects between these 3 types of outcome measures and the two forms of Goal Management Training were found. Irrespective of treatment, performance improved on two executive tests (Modified Six Elements Test; \( p=0.006 \), Zoo Map test; \( p=0.001 \)) and daily executive function problems as reported by the participants (EFI; \( p=0.001 \)) and proxies (DEX; \( p=0.01 \)) diminished. Our previous findings had shown that the addition of errorless learning to traditional Goal Management Training resulted in superior results when training everyday tasks. Improvements in cognition and quality of life, however, do not differ between the two treatments.

Introduction

Goal Management Training (GMT, Robertson, 1996) is a cognitive rehabilitation intervention for brain-injured persons with executive impairments aimed at training complex everyday activities. These patients, who experience problems with goal-directed behavior, are taught to apply an algorithm through which everyday tasks are subdivided into multiple steps. The main aim is to teach patients to ‘stop and think’ after each completed task step in order to monitor performance and to maintain the end goal of the task actively in working memory (Levine et al., 2000). Previous studies have shown that GMT is effective, especially in combination with other rehabilitation interventions, such as problem solving therapy (Krasny-Pacini, Chevignard, & Evans, 2014). Another approach to the training of daily tasks is errorless learning. Here, the occurrence of errors is prevented during the learning of task steps (Baddeley, 1992). Although the effectiveness of errorless learning has been established in amnesic patients (e.g., in Alzheimer Dementia it may also be beneficial for executively impaired patients. These patients have problems with error-monitoring and difficulties in adjusting behavior on the basis of feedback (Clare & Jones, 2008).

Our recently published RCT (Bertens, Kessels, Fiorenzato, Boelen, & Fasotti, 2015) was the first in which errorless learning and GMT were combined. The study showed that this combination resulted in a larger improvement of performance in self-chosen everyday tasks compared to GMT only. In this study we investigate additional parameters. The aim is to examine whether errorless GMT also contributes to improvements of cognitive function, as measured with neuropsychological tests, and subjective cognitive function along with quality of life assessed with questionnaires. Although our trial was aimed at improving self-chosen everyday tasks, the results may generalize to ecologically valid executive function tests. Moreover, we hypothesize that improved everyday function may contribute to a reduction of cognitive complaints and a better quality of life.

Methods

The treatment protocol has been published elsewhere (Bertens, Fasotti, Boelen, & Kessels, 2013). In short, patients with executive deficits due to acquired brain injury of non-progressive nature were recruited from four rehabilitation centers between 2012 and 2014. Participants gave written informed consent before engaging in the study and all data were obtained in compliance with the Helsinki Declaration. The study is approved by the Medical Review Ethics Committee region Arnhem-Nijmegen (reference NL38019.091.11) and registered at the Netherlands Clinical Trials Registry (reference no. NTR3567).
Procedure and interventions
Both the experimental errorless and the conventional GMT comprised 8 one-hour individual sessions, administered twice a week by trained therapists. In the first two sessions, identical for both treatment arms, two treatment goals (i.e., self-chosen everyday tasks) were selected. After session 2, baseline assessment took place in which the patient performed both tasks. This performance was videotaped and rated by assessors who were blind for treatment condition. The patients were randomly allocated to one of the treatment conditions using computerized block randomization. In errorless GMT, both the acquisition and application of the GMT strategy, including learning and performing the task steps, were taught using error reducing methods such as verbal and written instructions, cue cards and modeling. In contrast, during conventional GMT trial-and-error learning was allowed. In this condition the trainer did nothing to prevent errors, but only provided feedback in response to errors. Although patients were encouraged to apply the GMT and perform task steps, the trainer did not intervene to define or prompt task steps. After treatment the performance of both everyday tasks was again videotaped and rated.

Outcomes
Nine neuropsychological tests assessing executive and memory function as well as attention and concentration (see Bertens et al. (2013) and Table 1 for test details) were administered as part of the recruitment procedure. Everyday executive complaints and problems were assessed in both the patients and their proxies using the Dysexecutive Questionnaire (DEX). To measure self-reported cognitive and executive complaints patients also completed the Cognitive Failures Questionnaire (CFQ) and the Executive Function Index (EFI). Proxies completed the Executive Observation Scale (EOS) as an observational measure for executive function (see Bertens et al. (2013) and Table 2 for details). Quality of life was evaluated with the RAND-36 (see Bertens et al. (2013) and Table 3). All questionnaires and tests were also administered after treatment, using parallel versions if applicable.

Analyses
GLM repeated measures analyses were used to examine the effects of the interventions on neuropsychological test and questionnaire results. Alpha was set at 0.01 to correct for multiple testing. For the neuropsychological tests, regression-based Reliable Change Indices (RCI) were computed that take non-systematic measurement errors and systematic practice effects into account, using the computer program RegBuild_MR.exe (Crawford, Garthwaite, Denham, & Chelune, 2012; http://homepages.abdn.ac.uk/j.crawford/pages/dept/RegBuild_MR.htm) and test-retest data (means, standard deviations and correlations) derived from the test’s manuals. The percentage of patients who showed a reliable improvement was calculated using the RCI results.

Results
Sixty of the initially included 67 participants completed the trial and received errorless (n=30) or conventional GMT (n=30). Treatment effects on the primary and secondary outcome measures have been reported elsewhere (Bertens et al., 2015). Briefly, everyday task performance (primary outcome) improved significantly more after errorless GMT compared to conventional GMT (p=.006, Cohen’s $d=0.87$). Goal attainment scored by the trainers showed also a superior effect of errorless GMT (secondary outcome). Demographic characteristics and type and duration of brain injury did not differ between the two groups, nor did objective and subjective cognitive function and quality of life at baseline (Bertens et al., 2015).

Table 1 shows the neuropsychological test scores at baseline and post-training. No significant group by time interaction effects were found. Overall, participants improved significantly on the MSET ($F(1,50)=8.14, p=.006, \eta^2_p=0.14$) and Zoo Map test ($F(1,48)=17.42, p<.001, \eta^2_p=0.27$). RCI analyses showed that none of the participants reliably improved on the MSET after training. On the Zoo map test, 20.0% of the patients (errorless GMT: 18.5%; conventional GMT: 21.7%) improved reliably after training.

Furthermore, subjective cognitive complaints did not interact with type of treatment either (Table 2). Overall, executive everyday function as reported by the patients increased (DEX: $F(1,49)=13.58, p=.001, \eta^2_p=0.22$) and executive behavioral problems reported by proxies decreased (DEX: $F(1,47)=7.97, p=.007, \eta^2_p=0.15$). No significant changes on quality of life were found (Table 3).
Table 1  Mean (SD) for neuropsychological tests (objective cognitive functions) before and after treatment by treatment condition and outcome changes.

<table>
<thead>
<tr>
<th>Errorless learning GMT</th>
<th>Conventional GMT</th>
<th>Main eff time</th>
<th>Main eff condition</th>
<th>Interaction</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre</td>
<td>Post</td>
<td>Pre</td>
<td>Post</td>
</tr>
<tr>
<td></td>
<td>Mean (SD)</td>
<td>N</td>
<td>Mean (SD)</td>
<td>N</td>
</tr>
<tr>
<td><strong>Executive function</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Response generation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CFT</td>
<td>31.43 (7.24)</td>
<td>29</td>
<td>32.70 (8.15)</td>
<td>28</td>
</tr>
<tr>
<td>LFT</td>
<td>26.28 (8.56)</td>
<td>30</td>
<td>28.86 (9.57)</td>
<td>27</td>
</tr>
<tr>
<td><strong>Response inhibition</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Go/no-go Planning</td>
<td>676.43 (93.28)</td>
<td>30</td>
<td>656.52 (133.80)</td>
<td>25</td>
</tr>
<tr>
<td><strong>Working memory</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MSET</td>
<td>4.00 (1.78)</td>
<td>30</td>
<td>4.71 (1.51)</td>
<td>28</td>
</tr>
<tr>
<td>Zoo map</td>
<td>5.33 (4.62)</td>
<td>30</td>
<td>8.44 (6.38)</td>
<td>27</td>
</tr>
<tr>
<td><strong>Memory</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RBMT (z-score)</td>
<td>2.61 (.14)</td>
<td>30</td>
<td>2.89 (.13)</td>
<td>29</td>
</tr>
<tr>
<td><strong>Attention &amp; concentration</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alertness</td>
<td>365.59 (71.14)</td>
<td>29</td>
<td>329.38 (114.10)</td>
<td>26</td>
</tr>
</tbody>
</table>

Notes. CFT= Category Fluency Test; LFT= Letter Fluency Test; Go/no-go= Go/no-go, subtask TAP 2.1 (median); MSET= Modified Six Elements Test; Zoo map = Zoo map test, subtask of Behavioural Assessment of the Dysexecutive Syndrome; LNS= Letter Number Sequencing, subtask of Wechsler Adult Intelligence Scale-third edition; Brixton= Brixton Spatial Anticipation Test; RBMT (3)= Rivermead Behavioural Memory test (third edition); Alertness= Alertness, subtask TAP 2.1 (median); F and P values represent the main effects of time (baseline, post intervention) and condition (errorless learning GMT, conventional GMT) and the interaction effect between condition and time. P value ≤ .01 is used as statistical significance.

Table 2  Mean (SD) for questionnaires (subjective cognitive functions) before and after treatment by treatment condition and outcome changes.

<table>
<thead>
<tr>
<th>Errorless learning GMT</th>
<th>Conventional GMT</th>
<th>Main eff time</th>
<th>Main eff condition</th>
<th>Interaction</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre</td>
<td>Post</td>
<td>Pre</td>
<td>Post</td>
</tr>
<tr>
<td></td>
<td>Mean (SD)</td>
<td>N</td>
<td>Mean (SD)</td>
<td>N</td>
</tr>
<tr>
<td><strong>Cognitive complaints</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CFQ</td>
<td>87.07 (14.42)</td>
<td>29</td>
<td>88.73 (11.03)</td>
<td>30</td>
</tr>
<tr>
<td><strong>Executive behavioural problems</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DEX patient</td>
<td>27.59 (11.15)</td>
<td>29</td>
<td>25.10 (8.99)</td>
<td>30</td>
</tr>
<tr>
<td>DEX proxy</td>
<td>29.96 (11.50)</td>
<td>28</td>
<td>24.86 (13.15)</td>
<td>28</td>
</tr>
<tr>
<td>DEX difference</td>
<td>2.39 (14.77)</td>
<td>28</td>
<td>-0.50 (11.68)</td>
<td>27</td>
</tr>
<tr>
<td><strong>Self-reported executive function</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EFI</td>
<td>95.89 (9.43)</td>
<td>27</td>
<td>98.33 (10.04)</td>
<td>30</td>
</tr>
<tr>
<td><strong>Observed executive function</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EOS</td>
<td>23.33 (5.37)</td>
<td>21</td>
<td>25.00 (4.25)</td>
<td>25</td>
</tr>
</tbody>
</table>

Notes. CFQ= Cognitive Failures Questionnaire; DEX= Dysexecutive Questionnaire; EFI= Executive Function Index; EOS= Executive Observation Scale; F and P values represent the main effects of time (baseline, post intervention) and condition (errorless learning GMT, conventional GMT) and the interaction effect between condition and time. P value ≤ .01 is used as statistical significance.
Discussion

The current study did not reveal beneficial effects of errorless GMT on cognitive function and quality of life compared to conventional GMT. Independent of treatment type, improvements on the MSET and the Zoo map test were found. A reliable improvement, however, was only found for the Zoo Map scores in 20% of the patients. The remaining executive tests did not reliably improve. Improvement on the Zoo Map test could reflect a transfer effect to an untrained, yet ecologically valid executive task. A previous GMT study in brain-injured patients (Levine et al., 2011) also found transfer to an untrained Go/No-go task (SART) and a visuospatial planning task (D-KEFS Tower Test).

With respect to subjective cognitive complaints, no differences were found between the errorless and the conventional GMT groups after treatment. In general, patients reported better executive function in daily living after both treatments, whereas proxies reported a decrease in executive behavioral problems. This is in agreement with the results of previous studies, which also showed that proxies (Miotto, Evans, De Lucia, & Scaff, 2009; Schweizer et al., 2008; Spikman, Boelen, Lamberts, Brouwer, & Fasotti, 2010; Spikman et al., 2010) reported less complaints after GMT. However, in our study post-treatment improvements were not found on all subjective cognitive measures.

Finally, no significant changes on self-reported quality of life were found. This indicates that treatment and the improvement of specific daily activities did not affect the patients’ wellbeing in either treatment condition. Possibly, the time to benefit from possible training gains was too limited, as the assessment took place directly after training. Longer follow-up assessments could overcome this particular issue. Another limitation of our study design is that no untrained control group was included. The reported improvements could, as a result, be ascribed to extraneous variables such as natural recovery. However, by only including brain-injured patients in the chronic phase, natural recovery was not expected.

In conclusion, extending our previous findings (Bertens et al., 2015), we argue that errorless GMT contributes to a more effective training of daily activities, yet does not show additional transfer to untrained executive tests nor affects subjective performance and quality of life to a greater extent than conventional GMT. Irrespective of treatment, we observed improvements, albeit limited ones, concerning executive function and complaints, which are in line with previous research. The combination of errorless learning and GMT is a valuable contribution to cognitive rehabilitation enhancing performance of specific everyday tasks.
Seven Predictors of everyday task improvement after errorless Goal Management Training in brain-injured persons with executive deficits

Published as:
Abstract

The aim of this study was to identify moderators, mediators and predictors of outcome, that is, everyday task performance at the end of an experimental combination of errorless learning and Goal Management Training. Sixty patients with acquired brain injury of non-progressive nature with a minimal post-onset time of 3 months completed an RCT in which they were randomly allocated to 8 sessions of errorless or conventional Goal Management Training. The main outcome measure was everyday task performance, assessed at baseline and after treatment by evaluating correct, ineffective and missing task steps. In an exploratory regression analysis, demographic variables, neuropsychological test performance, subjective cognitive function and quality of life were tested as candidate predictors. The results showed that age ($p = .03$) and estimated IQ ($p = .02$) emerged as moderators. Higher age was associated with better everyday task performance following conventional Goal Management Training whereas higher IQ was associated with better performance following errorless Goal Management Training. Higher executive function scores after training predicted improved everyday task performance across the two treatment conditions ($p = .04$). The identified predictors may contribute to a more tailored cognitive rehabilitation approach in which treatments and patients are better matched when clinicians decide to train everyday tasks.

Introduction

Many individuals with acquired brain injury experience difficulties when performing daily life activities due to problems with formulating goals and planning and initiating behavior (Damasio, 1995; Duncan, Emslie, Williams, Johnson, & Freer, 1996; Stuss & Levine, 2002). These executive deficits are commonly observed in persons with brain injury referred for outpatient rehabilitation (Cicerone et al., 2000). Because even subtle executive impairments may have an impact on everyday functioning (McDonald, Flashman, & Saykin, 2002), investigated interventions aimed at overcoming these problems have been developed (Boelen, Spikman, & Fasotti, 2011). A well-studied intervention is Goal Management Training (GMT; Robertson, 1996) in which a cognitive strategy is practiced in order to keep a goal (i.e., a complex daily task) and its corresponding subgoals and task steps actively in working memory. Patients are taught to monitor their own performance by using an algorithm in which not only the task steps are carried out, but also ‘checking’ moments after each task step are trained to increase cognitive control (see Levine et al. (2000) for a more detailed description). The application of GMT in individuals with brain injuries has been evaluated in several studies. In general, positive effects have been reported on self-report questionnaires, standardized cognitive tests (Levine et al., 2011; Manly, Hawkins, Evans, Woldt, & Robertson, 2002; Miotto, Evans, Lucia, & Scaff, 2009) as well as on real-life activities, such as financial management (Grant, Ponsford, & Bennett, 2012) and meal preparation (Levine et al., 2000). Recent evidence suggests that combining GMT with other training methods may increase its effectiveness (Krasny-Pacini, Chevignard, & Evans, 2014).

Recently, we performed an RCT to investigate the efficacy of GMT and errorless learning on everyday task performance in individuals with brain injury. This combined approach was compared to conventional GMT (Bertens, Kessels, Fiorenzato, Boelen, & Fasotti, 2015). Errorless learning refers to the prevention of errors that occur during task acquisition in contrast to traditional trial-and-error learning in which errors occur naturally (Baddeley, 1992). The main aim was to train two individually selected everyday tasks (e.g., meal preparation, online banking, cleaning a room). Thirty participants received the experimental combination of GMT and errorless learning whereas 30 participants received conventional GMT. Those who were administered the experimental errorless GMT improved to a larger extent on everyday task performance than the participants who only received conventional GMT in the absence of any baseline differences between the two groups.

Although the evaluation of the efficacy of treatments is important, it is also (clinically) relevant to investigate for whom or under what conditions a treatment
works (i.e., moderators of treatment outcome; Baron & Kenny, 1986) and through which possible mechanisms beneficial effects are achieved (i.e., mediators of treatment outcome; Kraemer, Wilson, Fairburn, & Agras, 2002). Knowledge concerning patient characteristics that predict or moderate improvement in everyday life activities could contribute to a more tailored approach and thus to more effective and efficient rehabilitation treatments. Although the efficacy of GMT interventions or errorless learning have been studied previously, predictors for treatment success have not been reported.

The main aim of the current study is to identify mediators and moderators of treatment outcome (i.e., everyday task performance) in the above described RCT. For the present analyses, we followed the guidelines of Kraemer et al. (2002) for analyzing mediators and moderators in randomized clinical trials. Since studies investigating predictors in GMT and errorless learning are lacking altogether, we adopted a hypothesis-generating approach with an exploratory analysis. We selected several variables as possible predictors that could generate specific hypotheses for predicting treatment success.

Methods

Procedure

The protocol and rationale of the RCT were described in detail (Bertens, Fasotti, Boelen, & Kessels, 2013) and the effects on primary and secondary outcome measures were published elsewhere (Bertens et al., 2015). Four outpatient rehabilitation centers participated in the study (Rehabilitation Medical Centre Groot Klimmendaal, Arnhem, and Sint Maartenskliniek, Nijmegen, the Netherlands and Don Calabria, Verona, and Daccapo, Padua, Italy). All participants were aged between 18 and 70, lived independently at home and had executive impairments due to acquired brain-injury (> 3 months post injury). The study is registered at the Dutch Trial Register (reference NTR3567) and approved by the Medical Review Ethics Committee region Arnhem-Nijmegen (reference NL38019.091.11). Participants gave written informed consent before engaging in the study and data were obtained in compliance with the Helsinki Declaration. Executive impairments were assessed using an extensive neuropsychological test battery, including seven executive function tests. Specifically, patients were included when they either performed >1.5 standard deviation (SD) below the normative mean on at least two of the seven executive tests or between 1 and 1.5 SD below the normative mean on at least four of those seven tests. Moreover, memory and attention were assessed. Exclusion criteria were neurodegenerative disorders, substance abuse, severe premorbid psychiatric problems or severe cognitive comorbidity. Participants were randomly assigned to one of the two treatment conditions (conventional GMT or the experimental combination of GMT with errorless learning) using a computerized block randomization procedure with a block size of 4. Sixty participants completed the study. The first two training sessions were identical for both treatment arms. During the second session two individually chosen treatment goals (i.e., everyday tasks, such as cleaning a room, preparing a meal and conducting an online transaction; for an overview see Bertens et al., 2015) were selected by each participant. The remaining six sessions were dedicated to the training of these tasks. Execution of each task was filmed and assessed at baseline (after the second session) and after training. Neuropsychological assessment, consisting of parallel forms of the same tests when applicable, was administered after treatment as well. Moreover, participants and their proxies completed several questionnaires at baseline (before the videotaping of each task) and after treatment.

Treatments

The aim of both treatments was the training of two individually selected treatment goals, namely the successful completion of everyday tasks such as cleaning a room, preparing a meal, or conducting an online banking transaction. Both interventions consisted of a form of Goal Management Training including the use of information texts and (exercise) schemes, developed by the researchers and based on its original clinical manual (Robertson, 1996). Both interventions consisted of eight one-hour individual sessions given twice a week by trainers, either trained occupational therapists or psychologists. The first four sessions took place in the participating centers whereas the remaining four sessions were carried out at the participants’ homes. The two treatments are described in detail elsewhere (Bertens et al., 2013). Briefly, in conventional GMT patients were taught a strategy to keep the selected everyday goal and the corresponding task steps active in working memory. Patients were trained to monitor their performance during the execution of the task steps and to check if they were still aware of all further steps that led to the goal (Levine et al., 2000). GMT was combined with errorless learning in the experimental condition. Here acquisition as well as execution of task steps were trained using errorless learning techniques such as the use of visual and verbal (feed-forward) instructions and cue cards (De Werd, Boelen, Olde Rikkert, & Kessels, 2013).

Moderators, mediators and non-specific predictors

In our exploratory analysis, demographic characteristics, baseline neuropsychological test performance, baseline subjective cognitive complaints and baseline quality of life were selected as possible moderators. The post-treatment scores of
neuropsychological tests and self-report questionnaires were included as possible mediators (see also Tables 1 and 2).

The demographic variables included age, sex, years of education, brain injury (stroke, traumatic brain injury, or other), location of brain injury, and time between brain injury and assessment (in months), estimated IQ (measured with the National Adult Reading Test; NART; Nelson & O’Connell, 1978). Neuro-psychological assessment covered the domains executive function, memory and attention. Executive function was assessed using seven widely used and well validated neuropsychological tests, including Letter and Category Fluency (Schmand, Groenink, & Van den Dungen, 2008); a Modified Six Elements Test (MSET; Bertens, Frankenmolen, Boelen, Kessels, & Fasotti, 2014); the Zoo Map test (Wilson, Alderman, Burgess, Emslie, & Evans, 1996); Letter-Number Sequencing (Wechsler, 1997); the Go/No-go subtest of the Test for Attentional Performance (TAP) 2.1; Zimmermann & Fimm, 2007) and the Brixton Spatial Anticipation Test (Burgess & Shallice, 1997). To ensure that higher scores represented better performance, the reaction times of the Go/No-go task were multiplied by -1 and correct responses were computed for the Brixton test. A mean executive domain score was computed by calculating the mean of the z-scores of the individual tests. Memory was assessed with the Rivermead Behavioural Memory Test (RBMT; Wilson, Cockburn, Baddeley, & Hiorns, 1989; n=12) or the RBMT-3 (Wilson et al., 2008; n=48). As two versions of the RBMT were used, standardized scores were used to compute the z-scores. Attention was evaluated with the Alertness subtest of the computerized TAP 2.1 (Zimmermann & Fimm, 2007). The mean score for the medians of the reaction times on both the condition with and without alarm tone was computed. Self-reported daily executive skills were measured with the Executive Function Index (EFI; Spinella, 2005) and subjective cognitive complaints were assessed using the Cognitive Failures Questionnaire (CFQ; Broadbent, Cooper, Fitzgerald, & Parkes, 1982). The Dysexecutive Questionnaire (DEX; Wilson et al., 1996) was used to assess the level of awareness of executive dysfunction by subtracting the percentage scores using the theoretical number of steps (determined by the assessor) that were needed for task completion, allowing statistical comparison between different tasks. Since each participant had selected two everyday tasks, one mean percentage of the two treatment goals was calculated. The performance of the everyday tasks was filmed at baseline (after the second session in which the tasks were selected) and immediately after training.

Statistical analyses
To test whether the candidate variables were predictors (i.e., moderators, mediators or non-specific predictors) univariate GLM analyses were used. Post-treatment Everyday task performance ratings were the dependent variable, whereas baseline values of the outcome measure, the candidate predictor (grand-mean-centered), treatment group (errorless or conventional GMT) and the predictor-by-treatment group interaction term were entered as independent variables. Post-hoc general linear models were used to further investigate the nature of significant predictors or interaction terms (Kraemer et al., 2002).

A baseline variable (including the demographic variables) was classified as a moderator in case of a significant interaction effect between this variable and the treatment group. A post-treatment variable was classified as a potential mediator when it significantly correlated with treatment and either the main effect or the interaction effect was significant. Both baseline and post treatment variables were considered non-specific predictors if only the main effect is significant (without a significant correlation). These guidelines (Kraemer et al., 2002) were applied previously in exploratory analyses as well (Le Grange et al., 2014). Furthermore, effect sizes were calculated (partial eta squared; $\eta^2_{p}$) for interpreting the results. An effect size of $\eta^2_{p} = 0.01$ is considered as small, $\eta^2_{p} = 0.06$ the treatment may achieve its aim. If a variable neither interacts nor correlates with treatment but predicts outcome, it can be characterized as a non-specific predictor.
as medium and $\eta^2 = 0.14$ as large. Analyses were conducted using IBM SPSS statistics 20.0.

**Results**

The results of the RCT are described in detail elsewhere (Bertens et al., 2015). Briefly, sixty participants completed the study and both the conventional ($n = 30$) and the errorless GMT group ($n = 30$) improved on everyday task performance. The patients in the errorless GMT improved significantly more ($p = .006$) with a moderate to large effect size (Cohen’s $d = 0.74$). To summarize the demographic characteristics, 34 participants were men, mean age was 48.3 (SD 13.6; range: 18-77), mean for number of years of education was 11.3 (SD 2.9), and mean estimated NART IQ was 99.5 (SD 14.6). Thirty-two participants were stroke patients, 26 had had a traumatic brain injury, in one participant brain injury was the result of the resection of a glioma and one participant had sustained an autoimmune encephalitis. Mean post-onset time was 52.4 months (SD 93.0; range 3-534). Figure 1 shows a CONSORT diagram showing the flow of the participants through the trial.

**Table 1** shows the status of the candidate moderators (i.e., the baseline variables including the demographic variables) of everyday task performance after treatment. Age emerged as a moderator for treatment condition on everyday task performance after training, as measured with the video performance ratings. The results indicate that older participants responded better to conventional GMT in terms of everyday task performance [$F(1,27) = 5.17, p = .03; B = .53, t(1,27) = 2.27, p = .03$].

Estimated IQ was identified as a moderator for treatment condition post training, everyday task performance as measured by the video performance ratings. Results indicated that participants with higher IQ scores performed better after the combined errorless GMT in terms of everyday task performance [$F(1,27) = 5.28, p = .03; B = .52, t(1,27) = 2.30, p = .03$]. None of the candidate moderators were identified as non-specific predictors.

**Moderators, mediators and (non-specific) predictors of outcome**

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**Table 1** Predictors and moderators of everyday task performance at end of treatment.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Main effect variable</th>
<th>$p$</th>
<th>$\eta^2$</th>
<th>Interaction effect variable × treatment $p$</th>
<th>$\eta^2$</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>$F(1,55) = 0.36$</td>
<td>.55</td>
<td>.006</td>
<td>$F(1,55) = 4.76$</td>
<td>.03*</td>
<td>.128</td>
</tr>
<tr>
<td>ABI duration</td>
<td>$F(1,55) = 3.27$</td>
<td>.08</td>
<td>.056</td>
<td>$F(1,55) = 3.67$</td>
<td>.06</td>
<td>.003</td>
</tr>
<tr>
<td>ABI type</td>
<td>$F(1,55) = 0.07$</td>
<td>.36</td>
<td>.16</td>
<td>$F(1,55) = 0.00$</td>
<td>.99</td>
<td>.000</td>
</tr>
<tr>
<td>ABI localization</td>
<td>$F(1,55) = 0.32$</td>
<td>.56</td>
<td>.006</td>
<td>$F(1,55) = 0.00$</td>
<td>.99</td>
<td>.000</td>
</tr>
<tr>
<td>Education</td>
<td>$F(1,55) = 0.15$</td>
<td>.70</td>
<td>.003</td>
<td>$F(1,55) = 1.39$</td>
<td>.24</td>
<td>.025</td>
</tr>
<tr>
<td>NART-IQ</td>
<td>$F(1,52) = 0.03$</td>
<td>.86</td>
<td>.01</td>
<td>$F(1,52) = 5.31$</td>
<td>.02*</td>
<td>.006</td>
</tr>
<tr>
<td>Executive function (baseline)</td>
<td>$F(1,55) = 1.04$</td>
<td>.31</td>
<td>.18</td>
<td>$F(1,55) = 1.37$</td>
<td>.25</td>
<td>.024</td>
</tr>
<tr>
<td>Attention (baseline)</td>
<td>$F(1,52) = 2.10$</td>
<td>.15</td>
<td>.039</td>
<td>$F(1,52) = 0.35$</td>
<td>.56</td>
<td>.007</td>
</tr>
<tr>
<td>Memory (baseline)</td>
<td>$F(1,52) = 0.33$</td>
<td>.57</td>
<td>.006</td>
<td>$F(1,52) = 0.51$</td>
<td>.48</td>
<td>.010</td>
</tr>
<tr>
<td>EFi (baseline)</td>
<td>$F(1,51) = 0.24$</td>
<td>.63</td>
<td>.005</td>
<td>$F(1,51) = 0.68$</td>
<td>.41</td>
<td>.013</td>
</tr>
<tr>
<td>CFQ (baseline)</td>
<td>$F(1,53) = 3.10$</td>
<td>.03</td>
<td>.05</td>
<td>$F(1,53) = 0.68$</td>
<td>.42</td>
<td>.013</td>
</tr>
<tr>
<td>RAND-36 (baseline)</td>
<td>$F(1,51) = 0.09$</td>
<td>.77</td>
<td>.002</td>
<td>$F(1,51) = 0.48$</td>
<td>.49</td>
<td>.009</td>
</tr>
<tr>
<td>DEX (baseline)</td>
<td>$F(1,52) = 2.87$</td>
<td>.10</td>
<td>.052</td>
<td>$F(1,52) = 0.08$</td>
<td>.78</td>
<td>.002</td>
</tr>
</tbody>
</table>

Notes: ABI type = TBI, non-TBI; EFi = Executive Function Index (total score); CFQ = Cognitive Failures Questionnaire (total score); RAND-36 = 36-item Short Form Health Survey (total score); DEX = Dysexecutive Questionnaire (difference score (total patient score minus total proxy score)).
Discussion

This study examined moderators and mediators of treatment outcome in an RCT, in which a combination of errorless learning and GMT was compared to conventional GMT in individuals with brain injury. Age and IQ were found to moderate everyday task performance after training. More specifically, higher age was associated with better everyday task performance after conventional GMT, whereas a higher IQ was associated with better performance after errorless GMT. Moreover, executive function assessed after training (and not at baseline) predicted treatment outcome, indicating that changes in executive function may be a possible mechanism (i.e., a mediator) through which treatment success across the two treatment conditions is achieved (Kraemer et al., 2002).

Predictors have not been reported in previous studies investigating the efficacy of GMT. However, the finding that older adults benefit more from conventional GMT extends previous findings on GMT in older people. Both Van Hooren et al. (2007) and Levine et al. (2011) demonstrated that GMT in healthy older adults resulted in improved planning abilities and decreased executive failures compared to a waiting-list control group. However, to date no studies have directly compared GMT performance in young and older adults with brain injury. Future studies should examine in more detail what the optimal GMT procedure is in older adults compared to young adults.

The finding that higher IQ scores predict better performance following the combined errorless GMT but not after conventional GMT is somewhat surprising. On the one hand, one might argue that higher intelligence is especially beneficial for trial-and-error learning (applied in conventional GMT) and that this type of learning may appeal more to creativity and ingenuity. On the other hand, intelligence may be related to the ability to understand and follow instructions, which is important in errorless learning and in agreement with our findings. The role of premorbid intelligence should thus be studied in future GMT research.

Finally, executive function measured after treatment emerged as a mediator for treatment outcome, regardless of treatment type. Executive function at baseline did not predict treatment outcome, supporting the idea that a change in executive function during training mediated outcome, which may reflect a mechanism through which improved performance on everyday tasks was achieved. The relationship between executive functions and performance of daily activities is evident (see Lezak, Howieson, & Bigler, 2012; Shallice & Burgess, 1991; Worthington, 2005), and even subtle executive deficits may result in everyday life problems (McDonald et al., 2002). Consequently, improvements in executive function may also result in better performance of daily life activities. The majority of studies

<table>
<thead>
<tr>
<th>Variable</th>
<th>Main effect variable</th>
<th>$p$</th>
<th>$\eta^2_p$</th>
<th>Interaction effect variable $\times$ treatment</th>
<th>$p$</th>
<th>$\eta^2_p$</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Executive function (post treatment)</td>
<td>$F(1, 47) = 4.32$</td>
<td>.04*</td>
<td>.084</td>
<td>$F(1, 47) = 1.27$</td>
<td>.27</td>
<td>.026</td>
<td>Mediator</td>
</tr>
<tr>
<td>Attention (post treatment)</td>
<td>$F(1, 45) = 0.99$</td>
<td>.32</td>
<td>.022</td>
<td>$F(1, 45) = 0.44$</td>
<td>.51</td>
<td>.010</td>
<td>-</td>
</tr>
<tr>
<td>Memory (post treatment)</td>
<td>$F(1, 46) = 0.52$</td>
<td>.48</td>
<td>.011</td>
<td>$F(1, 46) = 3.12$</td>
<td>.08</td>
<td>.063</td>
<td>-</td>
</tr>
<tr>
<td>EFI (post treatment)</td>
<td>$F(1, 50) = 0.67$</td>
<td>.42</td>
<td>.013</td>
<td>$F(1, 50) = 1.08$</td>
<td>.31</td>
<td>.021</td>
<td>-</td>
</tr>
<tr>
<td>CFQ (post treatment)</td>
<td>$F(1, 50) = 3.34$</td>
<td>.07</td>
<td>.136</td>
<td>$F(1, 50) = 1.21$</td>
<td>.28</td>
<td>.024</td>
<td>-</td>
</tr>
<tr>
<td>RAND-36 (post treatment)</td>
<td>$F(1, 49) = 0.47$</td>
<td>.50</td>
<td>.009</td>
<td>$F(1, 49) = 0.50$</td>
<td>.95</td>
<td>.000</td>
<td>-</td>
</tr>
<tr>
<td>DEX (post treatment)</td>
<td>$F(1, 46) = 2.08$</td>
<td>.16</td>
<td>.043</td>
<td>$F(1, 46) = 2.38$</td>
<td>.13</td>
<td>.049</td>
<td>-</td>
</tr>
</tbody>
</table>

Notes. EFI = Executive Function Index (total score); CFQ = Cognitive Failures Questionnaire (total score); RAND-36 = 36-item Short Form Health Survey (total score); DEX = Dysexecutive Questionnaire (difference score (total patient score minus total proxy score)).
investigating the rehabilitation of executive disorders practice ‘naturalistic’ everyday tasks to assess treatment effects (Boelen et al., 2011). However, untrained tasks should also be included to investigate transfer effects rather than task-specific practice effects. In our RCT the seven executive function tests were ‘untrained’ tasks. Performance on the Modified Six Elements Test and the Zoo Map of the BADS (Behavioural Assessment of the Dysexecutive Syndrome; Wilson et al., 1996), improved significantly independent of treatment type. Further analyses using reliable change indices (RCI) showed that on the Zoo Map improvement was unrelated to practice effects for 20% of the participants (Bertens, Kessels, Boelen, & Fasotti, 2015). A previous study also showed transfer to untrained tasks (i.e., the Tower test) following GMT (Levine et al., 2011). These findings indicate that the successful acquisition of an executive GMT strategy may also contribute to better performance in general everyday executive functioning.

Study limitations
Although our sample size was comparable to that of other studies investigating (types of) GMT, it was relatively modest for conducting predictor analyses. Moreover, since previous research concerning prediction of treatment outcome following GMT is lacking, a broad range of variables was tested (i.e., not a selection based on previous studies) and a-priori power analyses could not be performed. Therefore, our approach should be considered an exploratory one, generating hypotheses to investigate in future studies. Moreover, our RCT did not include a follow-up assessment. Follow-up assessments are essential to establish the long-term treatment outcome and its predictors. Furthermore, each participant was assessed by only one of the three assessors, therefore the inter-rater reliability could not be determined. Another limitation is that participants could be included three months after injury; as a result, one could argue that spontaneous recovery cannot be fully ruled out. Moreover, duration of the brain injury also varied across individuals. Our study is the first to investigate moderator and mediators for treatment success following GMT. Investigating predictors for outcome may contribute to a more tailored approach of cognitive rehabilitation by better matching patients with treatment. Future research should investigate the generated hypotheses in more detail to optimize treatment outcome.

Conclusions
The present study identified age and estimated IQ as moderators for treatment outcome. Higher age was associated with better everyday task performance following conventional GMT and higher intelligence level with better performance after an errorless GMT. Moreover, executive function mediated treatment outcome independent from treatment type. These findings should be further investigated by including and testing candidate predictors in larger samples.
Eight Summary and discussion
The aim of this thesis was to improve both assessment and rehabilitation of executive dysfunction in brain-injured persons. More specifically, improvement of assessment of executive deficits was examined using an adapted version of, and a novel scoring method for a traditional neuropsychological test, the Modified Six Elements Test (MSET). With respect to rehabilitation treatment, a newly developed errorless Goal Management Training (i.e., a combination of errorless learning and Goal Management Training) for training brain-injured patients everyday tasks, was developed and investigated. In this final chapter, an overview of the main results and conclusions will be presented. In addition, strengths, limitations and suggestions for future research will be discussed. Finally, recommendations for clinical practice will be provided.

**Main findings**

**Assessment of executive dysfunction**

In chapter two, the reliability of two newly developed parallel versions of a Modified Six Elements Test (MSET) and a novel scoring index were investigated in healthy participants. Although a high variability in performance was found between the first and second administration, no systematical performance differences between the two test versions were present. These findings indicate that both parallel versions of the test are equivalent, thus allowing measurement of executive functioning over the course of time (e.g., before and after an intervention) without the bias of task specific learning effects. Moreover, the novel scoring method clearly reduced the occurrence of ceiling performances compared to the conventional scoring. Hence, the newly proposed scoring index is better able to detect mild executive deficits.

In chapter three, the adapted MSET was administered in brain-injured participants to investigate whether the novel scoring method was better able (in comparison to the traditional scoring) to discriminate between individuals with and without executive deficits, based on their performance on other well established executive tests. Only for the adapted scoring method both sensitivity (81%) and specificity (67%) were within a clinically useful range and an acceptable cut-off score could be determined. These findings show that the adapted scoring method of the MSET can be clinically useful in measuring executive deficits in individuals with brain injury.

**Rehabilitation of executive dysfunction**

Chapter four contained a detailed description of the rationale and study protocol of the main study of this thesis. It described how we combined errorless
learning and Goal Management Training, two methods that have been well studied separately and both shown to be effective. The study design described how the efficacy of our experimentally combined errorless Goal Management Training was investigated by comparing errorless and conventional Goal Management Training. This chapter was the starting point for the subsequent chapters, in which the results of this randomized controlled trial (RCT) were presented.

Chapter five focused on the results of the RCT described in chapter four. The main outcome measures were everyday task performance as rated by treatment-blinded assessors and goal attainment as rated by the brain-injured participants and their trainers. The combination of errorless learning and Goal Management Training resulted in a significantly larger improvement on individually selected everyday tasks compared to conventional Goal Management Training. Moreover, goal attainment as scored by the trainers showed a superior effect of errorless Goal Management Training as well. However, goal attainment as reported by the participating patients did not show a difference between the two treatment arms. On the one hand, this contrast between the patient and the trainer scores may be explained by the patients’ lack of insight leading to an overestimation of their levels of everyday functioning. On the other hand, the trainers, who were not blind for treatment condition, may have been biased resulting in an overly positive view of the combined errorless Goal Management Training. Our study is the first to show that errorless learning in combination with Goal Management Training improves everyday task performance in brain-injured patients with executive impairments.

The effects on additional study parameters were reported in chapter six. Here, we examined whether errorless Goal Management Training also contributed to improvements of objective cognitive function, measured with neuropsychological tests, and subjective cognitive function as well as quality of life assessed with questionnaires. The results showed no beneficial effects of errorless Goal Management Training on cognitive function and quality of life compared to conventional GMT. Independent of treatment type, improvements on the MSET and the Zoo Map test were found. However, a reliable improvement could only be established for the Zoo Map scores in 20% of the patients. This may reflect some transfer to an untrained, yet ecologically valid, executive task. Furthermore, patients reported better executive function in daily life after both treatment conditions and proxies reported a decrease in executive behavioral problems.

In chapter seven, it was examined which variables predicted treatment success, that is, everyday task performance after treatment. The results identified estimated IQ and age as moderators (i.e., indicating for whom or under what conditions a treatment works). Higher IQ was associated with better everyday task performance following errorless Goal Management Training, whereas higher age was related to improved performance after conventional Goal Management Training. Executive function potentially mediated (i.e., indicating through which possible mechanisms beneficial effects are achieved) treatment outcome, since higher executive function scores after training (and not at baseline) predicted improved everyday task performance across the two treatment conditions. Our analyses should be considered exploratory, contributing to generating hypotheses that could be investigated (i.e., tested) in future studies to better predict treatment success of (errorless) Goal Management Training.

General discussion

The first aim of the thesis was to improve the assessment of executive (dys)function using an adapted MSET. The MSET entails the use of unstructured and open-ended subtasks which better mimic everyday demands in comparison to traditional executive tests such as the Stroop Color-Word Test, the Wisconsin Card Sorting Test and the Tower of London test. Previous research (Renison, Ponsford, Testa, Richardson, & Brownfield, 2012) confirmed that the MSET could reliably predict everyday executive performance in individuals with traumatic brain injury, underlining that the MSET can be considered an ecologically valid tool. However, the test has some limitations that affect its applicability in clinical practice. Patients with mild executive impairments often perform at maximum levels (when using the conventional scoring method) and hence, mild executive deficits often remain undetected. Furthermore, the MSET is susceptible to task-specific learning effects (Jelicic, Henquet, Derix, & Jolles, 2001) and the test-retest reliability is poor (Wilson, Alderman, Burgess, Emslie, & Evans, 1996).

As a result, the task is less suitable for evaluating changes over time. A novel scoring method for the MSET was proposed, allowing the detection of mild executive deficits overcoming its so-called ‘ceiling effect’. This novel scoring index took the distribution of time spent on the six subtasks of the MSET into account in addition to the number of rule breaks. A more homogeneous distribution of time between the subtasks indicates better planning abilities. Our findings show that the proposed scoring index clearly reduced the occurrence of ceiling performances. Moreover, the new scoring index is better able to discriminate between executively impaired and executively intact brain-injured patients compared to the conventional raw score. However, when administered twice, a high variability in test scores was observed between the administrations. This may be explained by the fact that participants do not always show a similar distribution of time on two subsequent test occasions.
Optimizing the scoring of the MSET is important for the detection of mild executive deficits. Distribution of time during performance may be an important aspect of planning ability and hence a valuable contribution to the MSET. Still, the high variability is a disadvantage of the proposed scoring index in its current form, affecting its applicability in clinical practice.

To improve the MSET’s ability to measure executive (dys)function over the course of time, we developed two parallel versions. No systematic differences (i.e., systematically higher or lower scores) between these two versions were found, indicating that both versions of the test are interchangeable.

In summary, the newly developed scoring index and parallel forms improve the MSET’s ability to both detect mild deficits and to measure executive (dys)function over the course of time. However, some issues concerning these adaptations of the MSET remain open for discussion, further investigation and improvement.

The second aim of the thesis was to further improve the rehabilitation of executive impairments in brain-injured patients. Our findings show that by integrating an errorless learning approach into the strategy, the efficacy of Goal Management Training indeed improved. We are the first to show that preventing the occurrence of errors during a strategy training enhances the acquisition of everyday activities in executively impaired patients. This finding is obviously relevant for clinical practice, since errorless Goal Management Training can be implemented in cognitive rehabilitation settings for training brain-injured patients everyday tasks.

In addition to its clinical relevance, our research also provides a valuable scientific contribution to the theoretical basis underlying the mechanisms of errorless learning. Studies investigating errorless learning have predominantly been conducted in patients with memory impairments. These studies often refer to two possible frameworks relating the benefits of errorless learning to dysfunctional explicit memory processes. The first theory attributes the success of errorless learning in amnesic patients to a failing explicit memory system, while implicit memory is still intact (Baddeley & Wilson, 1994; Evans et al., 2000). Errors made during learning are not explicitly corrected, resulting in the implicit consolidation of incorrect memory traces. The second theory hypothesizes that the beneficial effects of errorless learning operate through residual explicit memory processes. It is argued that any learning observed in amnesia is only possible via the use of residual explicit memory (Graf & Schacter, 1985; Tailby & Haslam, 2003).

More recent literature suggests that there is a third potential mechanism underlying errorless learning. Errorless learning may benefit executively impaired patients as well, because these patients do not recognize errors due to a dysfunctional error-monitoring system (Clare & Jones, 2008). As a result, incorrect responses are not corrected and subsequently consolidated. Research investigating the efficacy of errorless learning in executively impaired patients is scarce and limited to case-studies (Cohen, Vyvissaker, Hamilton, Kemp, & Claiman, 2010; Pitel et al., 2006). A recent study (Fish, Manly, Kopelman & Morris, 2015) investigated whether errorless learning was effective for training prospective memory tasks as well. Prospective memory involves remembering to act upon previously formed intentions (e.g., pay a bill, take medication on time) and is thus closely related to the executive system. The study showed that errorless learning applied to the training of prospective memory tasks benefits future action. However, as most studies, this study was also conducted in patients with memory disorders. Our findings show that preventing the occurrence of errors during learning also enhances task performance in executively impaired individuals. This confirms the hypothesized beneficial effects of errorless learning in this population as well. The present findings underline that errorless learning is more broadly applicable than previously assumed. It is obvious that the effects of this learning principle are not restricted to memory rehabilitation, but also improve executive function. Hence, the merits of errorless learning serve considerably more patients with severe cognitive impairments. Future research should aim to further extend the scope of application of errorless learning as a general instructional method in cognitive rehabilitation.

**Strengths, limitations and future directions**

The randomized controlled trial presented in this thesis investigated the efficacy of errorless learning in patients with executive deficits, while previous errorless learning research has mainly been conducted in patients with memory disorders. Proving the efficacy of errorless learning in an executively impaired sample thus contributes to both cognitive rehabilitation methods for training everyday activities and to the literature concerning the underlying mechanisms of errorless learning. A major strength of the treatment study was that a tailored approach was used in which individually selected treatment goals were chosen by each patient, establishing the feasibility of errorless Goal Management Training for training all sorts of everyday activities. In contrast, previous studies investigating the efficacy of Goal Management Training used standardized (laboratory) tests, questionnaires or one or two fixed daily tasks (selected by the researchers).

Several limitations have to be discussed and several issues should be investigated further in future research. First, no follow-up assessment was...
Management Training could be implemented in clinical practice and used in cognitive rehabilitation settings for training specific everyday activities. The training focused on specific tasks and did not aim at improvement of executive function in general, such as other comprehensive, and thus more time-consuming, treatments like the Multifaceted Treatment of Executive Dysfunction of Spikman, Boelen, Lamberts, Brouwer, & Fasotti (2010). Therefore, to ensure maximal profitability for patients, in our approach it is important to carefully choose treatment goals that are functionally important for each individual. As visualized in the International Classification of Functioning, Disability, and Health (ICF) Model (World Health Organization, 2001; Figure 1), training specific activities improves functional independence and leads to an enhanced participation and engagement in everyday life.

With respect to the assessment of executive function using the MSET, as mentioned above, normative data have to be collected before the novel scoring method can be implemented in clinical practice. When clinicians choose to use this scoring index, not only the amount of rule breaks has to be scored, the time spent on each subtasks has to be calculated as well. Although the time distribution is not used for the standard scoring of the MSET, the conventional scoring form (of the MSET as part of the Behavioural Assessment of the Dysexecutive Syndrome (BADS); Wilson et al., 1996) already requires to register the starting and ending times after each switch between subtasks and could thus be used for the novel scoring index. We also replaced the dictation subtask by a sorting task. This replacement makes the MSET more appropriate for the included in the treatment study (chapter five). Therefore, the maintenance of the treatment effect is unknown and future studies should investigate whether or not the superior everyday task performance after errorless Goal Management Training maintains over the course of time. Another limitation is that no untrained everyday tasks were included. Although transfer to untrained tasks may not be expected, one could argue that if the Goal Management Training algorithm was successfully acquired using an errorless (stepwise) approach, it may also be applied spontaneously to non-trained tasks. In chapter six an attempt was made to deal with this limitation by investigating whether reliable improvements on neuropsychological tests were observed. Although some of these used executive function tasks are considered to be ecologically valid, it is better to include ‘real-life’ everyday tasks. Therefore, future studies could further investigate whether untrained everyday tasks benefit from an errorlessly acquired goal management strategy as well. Although it could be considered a strength that predictors for treatment were investigated (see chapter seven), the used analysis was exploratory and thus generating hypotheses (instead of testing), limiting its clinical relevance. Future studies should test the generated hypotheses to confirm which patients benefit most from errorless Goal Management Training.

Regarding the assessment of executive dysfunction using the adapted MSET, Krasny-Pacini, Chevignard & Evans (2014) argued that our parallel forms did not overcome the ‘novelty problem’. An outcome measure needs to be novel to make significant demands on executive function. In our case, the content of the parallel forms is new, but the format is not. Furthermore, the aforementioned high variability between test-retest scores remains a weakness of the newly proposed scoring index. Future studies could investigate further modifications of the scoring method, for example by rating and incorporating the distribution of time spent on the subtasks using categories (e.g., poor, below average, average, good or excellent time distribution) instead of subtracting the shortest from the longest time spent on a subtask. Finally, before a novel scoring method can be implemented in clinical practice, normative data in larger samples varying in age, sex and educational level, should be collected.

**Doin’ it right in clinical practice**

Several clinical recommendations with reference to the assessment and treatment of executive impairments may be derived from the studies reported in this thesis. First, and probably most important, combining errorless learning and Goal Management Training enhances performance of everyday tasks in brain-injured patients with executive deficits. The investigated errorless Goal Management Training could be implemented in clinical practice and used in cognitive rehabilitation settings for training specific everyday activities. The training focused on specific tasks and did not aim at improvement of executive function in general, such as other comprehensive, and thus more time-consuming, treatments like the Multifaceted Treatment of Executive Dysfunction of Spikman, Boelen, Lamberts, Brouwer, & Fasotti (2010). Therefore, to ensure maximal profitability for patients, in our approach it is important to carefully choose treatment goals that are functionally important for each individual. As visualized in the International Classification of Functioning, Disability, and Health (ICF) Model (World Health Organization, 2001; Figure 1), training specific activities improves functional independence and leads to an enhanced participation and engagement in everyday life.

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**Figure 1** International Classification of Functioning, Disability, and Health (ICF) Model.
assessment of executive function in patients with language disorders. Furthermore, the two newly developed parallel versions are interchangeable and could be used in clinical practice for repeated testing (e.g., before and after an intervention).

It should be noted that executive functions tap the most complex and heterogeneous mental processes that human beings have at their disposal. Therefore assessing these processes requires more than the use of a single neuropsychological test. Multiple well validated tests are required to obtain a comprehensive profile taking the many facets of executive function into account. Furthermore, valid and reliable questionnaires (completed by both patients and proxies) and (structured) observations should complement executive testing if executive (dys)function is to be reliably mapped.

Conclusion

The studies presented in this thesis aimed to improve assessment and rehabilitation of executive dysfunction in brain-injured persons. The investigated adaptations to the MSET contribute to better possibilities to detect mild executive deficits and to evaluate executive function over the course of time. The studies examining the efficacy of combining errorless learning and Goal Management Training show that it enhanced the acquisition of everyday activities in executively impaired individuals. The findings confirm the previously proposed hypothesis (Clare & Jones, 2008) that errorless learning is not only beneficial for amnesic patients but for executively impaired patients as well. The investigated intervention contributes to an improved treatment of executive deficits and can be implemented in cognitive rehabilitation settings in clinical practice. When training brain-injured persons with executive deficits everyday tasks it is better to prevent the occurrence of errors. Applying that principle means that we are “doin’ it right” by “doin’ it right” (Daft Punk, 2013).


Evans, C., Margison, F., & Barkham, M. (1998). The contribution of reliable and clinically significant...


Problemen met het plannen, initiëren, organiseren en reguleren van doelgericht taakgedrag komen frequent voor bij patiënten met niet-aangeboren hersenletsel (NAH). Deze problemen vallen onder stoornissen in het cognitieve domein van de *executieve functies*. Executieve functies worden vaak omschreven als een paraplubegrip voor verschillende complexe cognitieve processen en subprocessen die nodig zijn om een bepaald doel (bijvoorbeeld in een alledaagse taak) te behalen. Traditioneel wordt aan de prefrontale hersengebieden een centrale rol toegekend bij allerlei executieve functies. Echter, deze prefrontale gebieden maken deel uit van neurale netwerken waar ook andere corticale en subcorticale gebieden bij betrokken zijn. Dit heeft tot gevolg dat ook hersenschade buiten de prefrontale gebieden kan leiden tot executieve stoornissen.

De meest objectieve manier om executieve stoornissen vast te stellen, is door het afnemen van neuropsychologische tests. Een bekende executieve test is de Vereenvoudigde Zes-elemententest. Deze test bestaat uit drie taken: *vertellen, plaatjes benoemen en rekenen*. Iedere taak bestaat uit twee delen (deel A en B). De patiënt wordt gevraagd om binnen tien minuten aan alle zes de delen te werken. Er is echter één regel waaraan men zich moet houden: het is niet toegestaan om tussen twee delen van dezelfde taak te wisselen. Zo mag er bijvoorbeeld na het werken aan *rekenen deel A* niet direct gewerkt worden aan *rekenen deel B*. Er moet dan eerst gekozen worden voor *plaatjes benoemen* (deel A of B) of *vertellen* (deel A of B). Een nadeel van de Vereenvoudigde Zes-elemententest is dat patiënten met milde executieve stoornissen relatief makkelijk de hoogst haalbare score halen. Hierdoor is de test niet geschikt voor het meten van milde stoornissen. Een ander nadeel is dat er leereffecten optreden als de test voor een tweede keer wordt afgenomen bij dezelfde patiënt. Hierdoor is de test niet geschikt voor het meten van voor- of achteruitgang van executief functioneren (bijvoorbeeld bij afname van de test voor en na een behandeling).

Naast diagnostische middelen beschikken therapeuten inmiddels ook over behandelingen om executieve stoornissen te verbeteren. Eén van die behandelingen is Goal Management Training. Deze training richt zich op het (opnieuw) aanleren van alledaagse taken, door gebruik te maken van een strategie waarbij patiënten leren om een taak op te delen in kleinere stappen en na uitvoering van iedere stap een ‘stop en controleer’ moment in te lassen. Tijdens deze momenten wordt er gecontroleerd of de stap goed is uitgevoerd en of de volgende stappen en het uiteindelijke doel nog duidelijk zijn.

Een andere techniek voor het aanleren van alledaagse taken is de *foutloos leren* methode. In tegenstelling tot het ‘meer gangbare’ *trial-and-error leren* mogen er bij foutloos leren geen fouten optreden tijdens het leerproces. Tijdens het
trainen van taken kan de therapeut fouten voorkomen door bijvoorbeeld instructies en cue kaarten te gebruiken of voordoen hoe stappen uitgevoerd moeten worden. Uit eerder onderzoek is bekend dat deze techniek goed werkt bij personen met dementie. Een mogelijke verklaring voor de werking van foutloos leren is gebaseerd op de veronderstelling dat een niet goed functionerend expliciet (bewust) geheugen de gemakte fouten niet opslaat en dus niet laat corrigeren. Niettemin wordt de gemaakte fout onbewust wel ingeprent, omdat het impliciete (onbewuste) geheugen nog relatief intact is. Hierdoor worden fouten als deel uitmakend van een handelingssequenti opgeslagen en niet verberpt. Het voorkomen van fouten tijdens het leerproces zou dit probleem omzeilen. Er zijn echter ook sterke aanwijzingen voor een ander werkingsmechanisme dat zou kunnen bijdragen aan een bredere inzet van foutloos leren. Dit mechanisme berust op problemen met de foutenmonitoring waarbij een patiënt een foute handeling niet als verkeerd opmerkt en dus ook niet als zodanig in het geheugen opslaat. Een beperkte foutenmonitoring wordt gezien bij patiënten met executieve stoornissen. Het lijkt dus aannemelijk dat de toepassing van foutloos leren niet alleen bij personen met geheugenstoornissen, maar ook bij personen met executieve stoornissen zinvol is bij het leren van alledaagse taken. Deze veronderstelling is echter nog niet voldoende onderzocht.

Diagnostiek van executieve stoornissen

In hoofdstuk 2 zijn twee nieuw ontwikkelde parallelversies van de Vereenvoudigde Zes-elemententest onderzocht bij gezonde deelnemers om te onderzoeken of beide versies na elkaar kunnen worden afgenomen om veranderingen in executieve functies over tijd te meten, zonder taakspecifieke leerreflecten. Daarnaast is een nieuwe scoringsmethode geïntroduceerd waarbij niet alleen de volgordefouten in acht werden genomen, maar ook de verdeling van de tijd over de zes delen van de test. Hoewel de variabiliteit tussen de scores op de twee parallelversies relatief hoog was, waren er geen structurele verschillen tussen de twee versies. Er werd dus niet structureel hoger of lager gepresenteerd op één van de twee versies. Dit wijst erop dat beide versies inderdaad na elkaar kunnen worden afgenomen zonder taakspecifieke leerreflecten. De nieuwe scoringsmethode kent ook geen plafondeffect, waardoor deze beter in staat is om milde executieve stoornissen te meten in vergelijking tot de oorspronkelijke scoringsmethode.

In hoofdstuk 3 is er één van de parallelversies van de aangepaste Vereenvoudigde Zes-elemententest afgenomen bij patiënten met niet-aangeboren hersenletsel. Het doel van dit onderzoek was om de oorspronkelijke scoringsmethode te vergelijken met de nieuwe scoringsmethode. Op basis van zes andere executieve tests was de groep deelnemers verdeeld in patiënten met en zonder executieve stoornissen. Vervolgens is onderzocht in welke mate beide scoringsmethoden van de Vereenvoudigde Zes-elemententest in staat waren om deelnemers met executieve stoornissen te detecteren. Uit de analyses bleek dat alleen voor de nieuwe scoringsmethode een afkappunt kon worden bepaald waarbij de sensitiviteit (81%) en de specificiteit (67%) voldoende waren om klinisch bruikbaar te zijn. Deze bevinding laat zien dat de nieuwe scoringsmethode, waarbij de verdeling van de tijd over de zes onderdelen wordt meegenomen, klinisch bruikbaar kan zijn voor het meten van executieve stoornissen bij personen met hersenletsel.

Revalidatie van executieve stoornissen


De voornaamste resultaten van deze studie worden gerapporteerd in hoofdstuk 5. De primaire uitkomstmaat was alledaagse taakuitvoering gemeten door middel van video-opnames van taakuitvoering voor en na de training. Met behulp van deze video-opnames werden correcte, inefficiënte en missende taakstappen gescend door beoordelaars die blind waren voor de behandelinconditie. De experimentele combinatie van foutloos leren en Goal Management Training resulteerde in een significant grotere vooruitgang op de individueel gekozen alledaagse taken in vergelijking tot de conventionele Goal Management Training. Een secundaire uitkomstmaat was Prozess Attainment Scale (GAS). Dit is een schaal waarin de deelnemende patiënten en de trainers afzonderlijk van elkaar konden aangeven in hoeverre de gekozen behandeldoelen werden behaald na de training. De GAS scores van de trainers lieten een superieur effect zien van de foutloze Goal Management Training. De GAS scores van de patiënten toonden echter geen verschil tussen de foutloze en conventionele Goal Management Training.

In hoofdstuk 7 is onderzocht welke variabelen een verbeterde alledaagse taakuitvoering voorspelden, zogenaamde predictoren voor behandel succes. Intelligentie en leeftijd werden geïdentificeerd als moderators. Een moderator voorspelt voor wie of onder welke omstandigheden een behandeling werkt. Een hogere intelligentie bleek gerelateerd aan een betere alledaagse taakuitvoering na de foutloze Goal Management Training. Een hogere leeftijd voorspeld een betere taakuitvoering na de conventionele Goal Management Training. Executief functioneren gebaseerd op zeven executieve tests en gemeten na de training voorspelde behandel succes in beide groepen en bleek dus een mogelijke mediërende variabele te zijn.

Tot slot wordt in de Algemene discussie (hoofdstuk 8) aandacht besteed aan de implicaties van bovengenoemde studies voor de klinische praktijk en de bijbehorende aanbevelingen voor toekomstig onderzoek. Er wordt geconcludeerd dat de studies in het huidige proefschrift bijdragen aan verbeteringen van zowel de diagnostiek als de behandeling van executieve stoornissen bij personen met niet-aangeboren hersenletsels. De veronderstelling dat de foutloos leren methode ook voordelig is voor personen met executieve stoornissen blijkt te kloppen. Het trainen van alledaagse taken bij patiënten met executieve stoornissen ten gevolge van niet-aangeboren hersenletsels werkt het best door gebruik te maken van foutloos leren.
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Het is af! Een heel karwei, maar dankzij de hulp van veel mensen vooral een leuk karwei!

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Publications

International publications


Published abstracts


Donders Graduate School for Cognitive Neuroscience Series


32. Van Dijk, J.P. (2010). On the Number of Motor Units. Radboud University Nijmegen, Nijmegen, the Netherlands.


38. Grootens, K.P. (2010). Cognitive dysfunction and effects of psychostimulants in schizophrenia and borderline personality disorder. Radboud University Nijmegen Medical Centre, Nijmegen, the Netherlands.


40. Kuribara, M. (2010). Synaptic potentiation and depression in the cerebellum and hippocampus. Radboud University Nijmegen Medical Centre, Nijmegen, the Netherlands.

41. Van der Spuy, B.C. (2010). Cerebral reorganization in Parkinson’s disease. Radboud University Nijmegen Medical Centre, Nijmegen, the Netherlands.


47. Van Grootel, T.J. (2011). Lexical access in speaking: Studies on lexical selection and cascading activation. Radboud University Nijmegen, Nijmegen, the Netherlands.


56. van der Linden, M.H. (2011). Experience-based plasticity in object category representation. Radboud University Nijmegen, Nijmegen, the Netherlands.


58. Everaerts, A. (2011). Synaptic potentiation and depression in the cerebellum and hippocampus. Radboud University Nijmegen Medical Centre, Nijmegen, the Netherlands.


61. Van Leeuwen, T.M. (2011). ‘How one can see what is not there’: Neural mechanisms of grapheme-colour synaesthesia. Radboud University Nijmegen, Nijmegen, the Netherlands.


64. Voerman, N. (2011). Motor unit discharges - Physiological and diagnostic studies in ALS. Radboud University Nijmegen Medical Centre, Nijmegen, the Netherlands.


