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Theoretical and Neurobehavioral Perspectives on Self-Awareness

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CHAPTER 1

General introduction

General Introduction

Acquired brain injury (ABI) refers to a sudden injury to the brain that occurs after birth and is unrelated to a congenital or neurodegenerative disorder. The most common causes of ABI are traumatic brain injury (TBI), due to an external force such as a fall or traffic accident, and stroke, due to occlusion or leakage of a blood vessel in the brain. However, ABI can also be caused by other brain disorders such as brain tumors, infections, or hypoxia after a cardiac arrest. In the Netherlands alone, approximately 650,000 people live with the daily consequences of ABI [1]. These consequences can differ per person and can consist of impairments in emotional, cognitive, physical, behavioral and psychosocial functioning [2, 3]. These impairments can be so severe that after receiving treatment in hospital, a substantial number of people need in- or outpatient rehabilitation treatment before they can return home [4].

According to clinical experts, one of the most important factors influencing the success of rehabilitation treatment is impaired self-awareness [5]. Impaired self-awareness generally refers to being unaware of impairments that are obvious to others [6]. Someone with impaired self-awareness after ABI has trouble assessing their strengths and weaknesses [7], which makes it difficult to understand the consequences of their ABI and the effects these have on themselves and (significant) others. Prevalence rates of impaired awareness in the ABI population are not well investigated, but estimates are that 7 to 77% of stroke patients and 30 to 50% of TBI patients show impaired self-awareness [7, 8]. This is a problem in rehabilitation treatment as people with impaired self-awareness often show low motivation, poor adherence to treatment, and are less likely to achieve their rehabilitation goals [9-12]. Furthermore, impaired self-awareness is associated with impaired emotion recognition [13] and poor rehabilitation outcomes such as less independent living skills [14, 15], worse long-term employment outcomes [16], social disturbances [17], and poor community re-integration [18]. Moreover, it is related to a high burden on relatives [19, 20].

Self-awareness and metacognition

If we say self-awareness is a cognitive function that is impaired after brain injury, there is an implicit assumption that unimpaired self-awareness also exists. Self-awareness is the ability to be conscious of your own thoughts, actions and cognition [21]. This ability has been studied in parallel in many fields of research such as neuropsychology, cognitive neuroscience, and education [23]. Self-awareness is an umbrella term that refers to awareness of one's functioning in any domain, such as the physical, cognitive, or emotional domain [17]. This thesis mainly concerns self-awareness of the cognitive domain, which is also called metacognition [22]. Therefore, throughout this thesis both of these terms will be used, with metacognition referring to self-awareness of the cognitive domain, specifically, which is a component of the broader concept self-awareness.

Metacognition in people without ABI

A recent review on metacognition in educational and cognitive neurosciences concluded there is a general distinction between online and offline metacognition [23]. Offline metacognition refers to slow and broad processes such as self-reflection. Brain regions involved in this type of metacognition are the prefrontal cortex, insula, precuneus, and parahippocampal gyrus [23]. Online metacognition, on the other hand, is fast, in-the-moment, and often very specific, such as confidence in isolated decisions [24]. Brain regions involved in online metacognition include medial frontal cortex, anterior cingulate cortex, and the prefrontal cortex [23]. Despite a consensus to distinguish online from offline metacognition, there are many different ways to measure metacognition that are used interchangeably and do not always make this separation between online and offline elements. Therefore, it is unclear how these measurement methods relate to the different elements of metacognition, and what the exact neural substrates are [23].

Models of impaired self-awareness after ABI

Two of the most influential models that describe impaired self-awareness after ABI are the pyramid model of awareness [25] and a more dynamic model [26]. Similar to the metacognition models in healthy people, the pyramid and dynamic model also consist of several elements. However, in these models self-awareness refers to awareness of an impairment in functioning due to the ABI. The pyramid model describes a hierarchy of three levels of awareness [27]. The first level is 'intellectual awareness' and refers to knowledge of the impairment. That is, someone knows or understands that they have difficulties with some activities or tasks. This level is a requirement for the second level, which is 'emergent awareness'. This is the ability to recognize a problem as it is happening. The highest level of awareness in this model is 'anticipatory awareness', which is the ability to anticipate that a problem could occur in the future. According to this model, someone must first know they have an impairment (intellectual awareness) and be able to recognize when the impairment causes problems (emergent awareness), before they can reach the highest level of awareness and prevent problems from occurring (anticipatory awareness).

The dynamic model of self-awareness after ABI consists of several elements that are not hierarchically related; instead they can all influence each other [26]. The main distinction made in this model is the difference between 'metacognitive knowledge' and 'online awareness'. Metacognitive knowledge refers to knowledge and beliefs related to oneself. This is rather stable, stored in long-term memory and, therefore, present prior to engaging in a task. Online awareness refers to knowledge and awareness that is activated during tasks or in certain situations. This relies heavily on the task and context. The dynamic element of this model refers to the assumption that pre-existing metacognitive knowledge can influence how someone perceives the task and forms expectations of performance on that task. The other way around, information gained during online awareness can strengthen or adjust prior beliefs in metacognitive knowledge.

The models described above do not distinguish between different causes of impaired self-awareness after ABI. For example, impaired self-awareness can be caused by neurocognitive factors, such as disrupted functioning of brain networks that are necessary for self-awareness, or it can be caused by psychological factors, such as denial of disability which serves as an emotional response to reduce anxiety [28]. The role of denial is often not addressed in studies of impaired self-awareness, which restricts knowledge on the effects of denial on rehabilitation of impaired self-awareness [28]. Furthermore, Prigatano and Sherer [28] argue that it is important to distinguish these two factors since they might require different therapeutic approaches.

Neural correlates of impaired self-awareness after ABI

Previous research suggests that injury-related factors play a role in the magnitude of impaired self-awareness. For example, some studies have found that more impaired self-awareness correlates with injury severity [29, 30], number of lesions [31], and location of these injuries [32, 33]. Generally, changes in self-awareness have been associated to frontal lobe damage [21]. However, these studies mostly examine TBI populations. Therefore, generalizability to other ABI populations remains unclear. Moreover, most of these studies are based on structural imaging. The few functional imaging studies that have been conducted suggest involvement of brain networks such as cortical midline structures [34], frontoparietal control network [35], and default mode network [36]. Imaging techniques have developed rapidly in the last decade but the studies on the functional neural correlates of (impaired) self-awareness after ABI lag behind. To help understand impaired self-awareness, build theoretical models, and improve treatments, it is important to understand what the neural substrates of impaired self-awareness are.

Measuring impaired self-awareness after ABI

A challenge in this field of research is how to measure self-awareness after ABI. The different measurement methods can generally be divided into four categories: clinician ratings, structured interviews, self-other rating discrepancy methods, and performance-based discrepancy methods [37]. Clinician ratings are ratings based on clinical judgment. Structured interviews can be conducted by clinicians or researchers to gain both quantitative and qualitative information on levels of self-awareness. For self-other discrepancy ratings, an ABI patient and 'other' person who knows the patient well (a significant other or therapist) both fill in a questionnaire about the patient's functioning. The 'other' scores are considered the objective measure to which the patient scores are compared. In performance-based discrepancy scores, (neuropsychological) test scores are used as objective measure and the ABI patient's prediction or evaluation of performance is compared to this score. For instance, a patient is given a memory task and is asked to predict how many items they expect to remember. Many measurement instruments have been developed. Some offline measures (such as Awareness Questionnaire [38], Patient Competency Rating Scale [39], and Self-Regulation Skills Interview [40]) are well validated while online measures, such as performance-based discrepancy scores, are less well validated. Furthermore, there are few instruments that assess denial of disability [28].

Treating impaired self-awareness after ABI

Several studies have shown positive effects of treatments on self-awareness after ABI. Some studies showed that a group therapy focused on psychoeducation about the brain, self-awareness, and coping [41] as well as a treatment including video feedback in combination with non-confrontational verbal feedback [42] successfully improved self-awareness after ABI. A systematic review by Schrijnemaekers et al. [43] showed that to improve self-awareness after ABI, treatments should include training skills in everyday settings along with multimodal feedback and dialogue between therapist and patient. A protocol including these elements was developed and tested in four single-case experimental designs. This Socratic feedback intervention deemed effective and feasible [44]. Two other treatments that seemed effective were a treatment including psychoeducation, strength and weakness analysis, predicting, monitoring and evaluating performance, goal setting, and planning [13], and a treatment including metacognitive strategy training with self-assessment and developing solutions [45]. However, despite these studies, several questions remain unanswered. For example, whether the protocols are truly effective to improve self-awareness as there was no control group [41] or there was a small sample size which reduces generalization [44].

Some treatments do not specifically aim to improve self-awareness, but aim to improve rehabilitation outcomes on the level of activities and participation despite self-awareness problems [46]. For example, a treatment in which patients had to estimate their performance before and after each task improved instrumental activities of daily living and self-regulation while there was no improvement in task-specific or general self-awareness [47]. A recent systematic review by Engel et al. [46] concluded that the promising elements of treatments aimed at improving activities and participation for people with impaired self-awareness after ABI are Socratic guided discussion, experiential task practice, feedback from multiple sources, and metacognitive strategy training.

It is encouraging that there are treatments that can improve self-awareness after ABI or that are effective in this population despite the self-awareness problems. However, more and larger controlled studies are necessary in order to define evidence-based guidelines for clinicians on how to deal with impaired self-awareness after ABI.

Aims and outline of this thesis

Impaired self-awareness following ABI is a commonly observed symptom and important clinical issue in rehabilitation treatment. However, it seems intangible and is not straightforward to treat or measure because it is a difficult concept to grasp. The aim of this thesis was to get a better understanding of impaired self-awareness following ABI. To achieve this, the following research questions were addressed:

1. How can different elements of self-awareness be measured?

   In chapter 2, we used different measurement methods to capture different aspects of metacognition in healthy subjects, and investigated how these correlated with one another. In chapter 5, we investigated psychometric properties of an instrument that can distinguish two main aspects of impaired self-awareness after ABI.

2. What are the neural correlates of metacognition in healthy subjects and ABI patients?

   In chapter 3, we investigated the functional neural correlates of making mistakes on a metacognitive task in healthy participants. In chapter 4, we systematically reviewed studies investigating structural and functional neural correlates of impaired self-awareness following ABI.

3. What is the nature and severity of impaired self-awareness following TBI?

   In chapter 5, we used the Clinician's Rating Scale for evaluating Impaired Self-Awareness and Denial of Disability after brain injury (CRS-ISA-DD) to investigate the nature and severity of impaired self-awareness in a community-dwelling TBI population. Furthermore, the impaired self-awareness and denial of disability subscales were correlated with injury-related, cognitive, and psychological measures.

4. How can rehabilitation outcomes be improved in ABI patients with impaired self-awareness?

   In chapter 6, we investigated the effectiveness of Socratic guided feedback on improving self-awareness and other short-term and long-term rehabilitation outcomes in a randomized controlled trial.

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CHAPTER 2

The Many Facets of Metacognition: Comparing Multiple Measures of Metacognition in Healthy Individuals

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Abstract

Metacognition is important for successful goal-directed behavior. It consists of two main elements: metacognitive knowledge and online awareness. Online awareness consists of monitoring and self-regulation. Metacognitive sensitivity is the extent to which someone can accurately distinguish their own correct from incorrect responses and is an important aspect of monitoring of behavior. Research into the interplay between these elements is currently lacking. Therefore, the aim of the current study was to explore how these different elements of metacognition can predict metacognitive sensitivity. Healthy participants filled out the Metacognitive Awareness Inventory with two subscales that serve as measures of metacognitive knowledge. Next, as measures of online awareness, they performed a memory task and an abstract reasoning task (that were adapted to include trial-by-trial confidence judgments), and made pro- and retrospective confidence judgments about their performance on these tasks. The 128 included participants show a large variability in scores on all the different metacognitive measures. On the memory task, metacognitive sensitivity was predicted by higher prospective discrepancy scores and lower retrospective discrepancy scores. For the abstract reasoning task, metacognitive sensitivity could not be predicted by the other variables, most likely due to the difficulty of the task. The current study confirms that metacognition is a multidimensional concept consisting of different elements. Online measures seem to be associated with each other, but not so much with offline measures. The current framework can be used to further investigate the associations between different elements of metacognition within persons.

Introduction

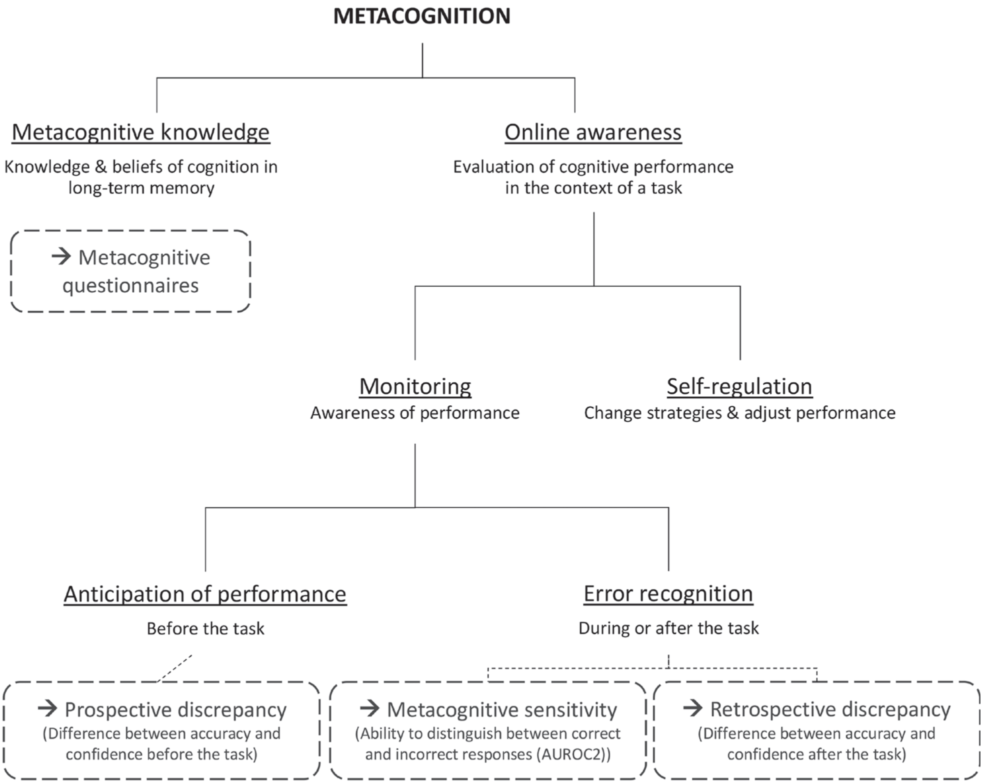
Metacognition is the ability to be conscious of your own thoughts, actions, and cognitions [1, 2]. We need to monitor and evaluate our cognition so we can adapt our behavior to achieve successful goal-directed behavior. As a topic of interest in multiple scientific fields such as neuropsychology, cognitive neuroscience, or education, more and more bridges are being made, which requires a calibration of constructs and measurement methods [3]. There are many ways to define the elements of metacognition that bring many discrepancies but also many overlaps [4]. One of the first classifications separated metacognitive knowledge, referring to knowledge and beliefs about factors influencing cognition, from metacognitive experiences, referring to conscious experiences related to a cognitive enterprise such as feelings of confusion [1]. Many models are based on this distinction between, on the one hand, a stable reflective knowledge of one's cognitive capacities and, on the other hand, a more "on the fly" online metacognition [3]. Another distinction can be made between local metacognition, such as confidence in isolated decisions, and global metacognition such as self-efficacy beliefs [5]. In an attempt to align different fields of research on metacognition, Fleur, Bredeweg [3] stress the need for more studies on protocols to measure the different constructs of metacognition and the relationships between these constructs.

Two main elements of metacognition, as described by a neuropsychological model of metacognition, are metacognitive knowledge and online awareness [6]. Figure 1 schematically represents an overview of these elements of metacognition. Metacognitive knowledge is knowledge and beliefs of one's cognitive processes and strategies that are stored in long-term memory. This knowledge base is gained over time and is rather stable, although it can be influenced and changed through successes and failures [6]. This is a common element in many models of metacognition since it was described by Flavell [1]. The other part of the model is online awareness and refers to evaluation of performance within the context of a task. This is more flexible as it depends on context and task characteristics such as complexity and familiarity of the task, as well as personal factors such as motivation and meaningfulness of the task [6]. This resembles "on the fly" metacognition [3] or metacognitive experiences [7]. In this model, online awareness consists of two elements. The first element is monitoring, which is awareness of performance within the context of a task. This includes anticipating performance after appraisal of task demands but before task completion, as well as error recognition during a task. The second element is self-regulation, which refers to the ability to change strategies and adjust performance in response to changing task demands and experience. These self-regulatory processes depend on accurate self-monitoring but also motivation and socio-emotional processes [4]. Intact metacognitive sensitivity is an important input for self-regulation and impaired metacognitive sensitivity could lead to incorrect or no behavioral adjustment. There are different measurement methods that can be related to the different elements of metacognition, these are also described in Figure 1.

Common ways of assessing metacognition are questionnaires and performance-based measures. Metacognitive questionnaires typically address situations either in the past or in the future, which trigger pre-existing knowledge and beliefs about one's cognition stored in long-term memory and, therefore, quantifies metacognitive knowledge. Examples of such questionnaires are the Metacognitive Awareness Inventory [8] and the Awareness of Independent Learning Inventory [9] which are both designed to assess self-reported metacognition in healthy adults. Online awareness can be quantified with performance-based measures. One way is using discrepancy scores between performance accuracy and confidence in one's performance [10]. For example, before or after a task someone can rate how well they think they will do or how well they have done. This can then be compared to actual performance accuracy, resulting in a prospective discrepancy score and retrospective discrepancy score, respectively. Anticipating performance before a task and evaluating performance after a task are based on different processes. Confidence judgments before a task (prospective confidence) are based on an analytic process of evaluating task demands and experiences [11], for which one might employ metacognitive knowledge. Confidence judgments after a task (retrospective confidence) are experience-based judgments that rely on experiences during a task such as feeling of knowing [11]. This judgment is given one time, after the task, and is an overall judgment of performance (e.g. this was a difficult task for me, I think I have not done well).

Another, more specific, measure of metacognition is metacognitive sensitivity [12]. This can be measured by asking participants during the task, after each trial, to indicate how confident they are that their answer is correct. Confidence and accuracy per trial is used to assess whether a person can differentiate correct from incorrect responses by applying signal detection theory [12]. When someone reports high confidence for correct answers and low confidence for incorrect answers, they are considered to have good metacognitive sensitivity [12]. Metacognitive sensitivity, as opposed to retrospective confidence, is less confounded by response bias [i.e. the tendency to always score high or low confident; 12].

Figure 1. Conceptual overview of metacognition based on previous literature.



Note. This figure provides a conceptual overview of metacognition. The arrows are the measurement methods to assess the different elements of metacognition, which are underlined. AUROC2 = type two area under the receiver operating characteristic curve.

The assessment of metacognition remains difficult and there is a demand for empirical evidence to support theoretical frameworks of metacognition and its different elements [5]. Moreover, there is a gap in the literature concerning the associations between the different constructs of metacognition [3]. Therefore, the aim of the current study was to explore how metacognitive sensitivity can be predicted by the different elements of metacognition, as measured by different measurement methods. The hypotheses are that smaller prospective and retrospective discrepancy scores (i.e. better metacognition) will be predict better metacognitive sensitivity, while metacognitive knowledge is expected to be positively associated with metacognitive sensitivity

Methods

Participants

Participants were 128 healthy volunteers (100 female, 27 male, 1 non-binary) who were 20.6 (±1.6) years old. They had a high school degree (N=102), associate degree (N=3), Bachelor's degree (N=19), or a Master's degree (N=4). Most were not native English speakers (N=116). Participants had to (1) be 19 up to and including 24 years old, (2) be able to give informed consent, (3) have a good comprehension of the English language, and (4) have access to and be able to use a laptop or computer with stable internet connection. Participants were excluded when they (1) had a history of, or a current, psychiatric illness or neurodegenerative disease, or (2) had a history of, or were currently under treatment for, alcohol or substance abuse. Participants were recruited through flyers at the university, social media, and a study participation system from Maastricht University. In order to reach a power of 0.80, with a significance level of 0.05, and a medium effect size of f^2=0.10, the aim was to include a minimum of 124 participants. Data were collected from April 2021 to January 2022.

Procedure

Participants completed the study from home in a single session that took about an hour. The main part of the study was administered via Qualtrics software (Qualtrics, Provo, UT). Figure 2 demonstrates the different steps of the study. When landing on the study website, participants read the information letter and signed informed consent online. If no consent was given, participants could not continue. The study started with a short demographics questionnaire that included age, sex, gender, handedness scale (for possible participation in future fMRI study), and level of education. Then a self-report metacognitive questionnaire was filled out. Subsequently, they performed a memory task and an abstract reasoning task as described below. There were no time limits set on any phase of the study. Some validity questions were entered throughout the session to ensure that participants took part in a serious manner. Ethical approval was obtained from the Ethics Review Committee Psychology and Neuroscience at Maastricht University with reference number OZL_233_21_02_2021.

Materials

Metacognitive Awareness Inventory (MAI)

This self-report questionnaire developed by Schraw and Dennison [8] consists of 52 items measuring metacognitive knowledge. Ratings for each item were made on a continuous scale ranging from 0 (completely false) to 100 (completely true). Psychometric analyses of this instrument show that it is a reliable instrument with high internal consistency [coefficient $\alpha = 0.88$ per subscale; 8].

Prospective and Retrospective Confidence Judgments

For both the memory task and abstract reasoning task, prospective confidence judgments about performance (after reading the instructions but before starting the task) and retrospective confidence judgments about performance (directly after completion of the task) were made. Participants had to indicate how well they thought they would perform (prospective) or had performed (retrospective) on the task on a scale from 0 to 10, where 0 corresponded to 'very bad' and 10 to 'very good'.

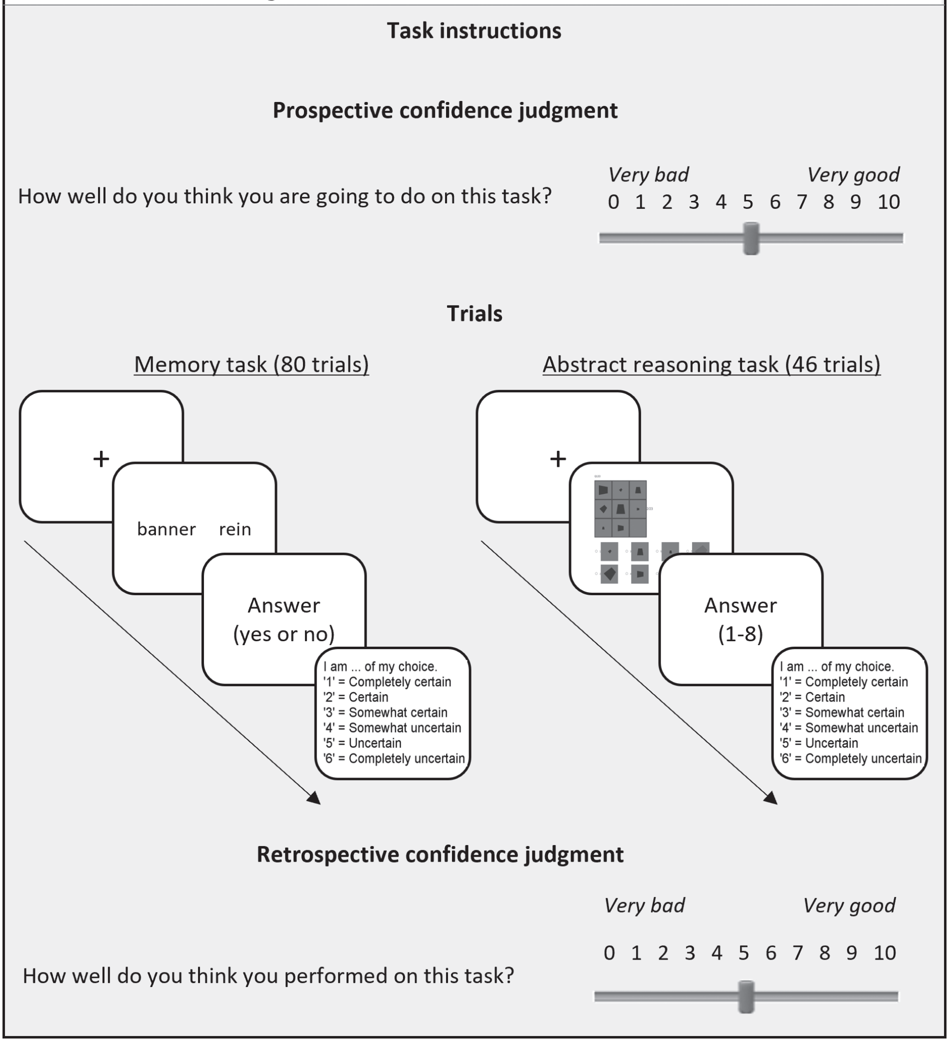
Memory Task

The memory task was a word pair learning task that was programmed and administered through Inquisit 6 [14]. The task consisted of two phases: an encoding phase and a recognition phase. During the encoding phase, participants were presented with 40 unrelated word pairs (cue word + pair) which were previously used and validated by Payne, Tucker [15; List 3]. Each word pair was displayed for 5 seconds and order of presentation was randomized for each participant. The recognition phase consisted of a two-alternative forced choice test. Participants were presented with 40 word pairs again. Cue words from the learned word pairs list were either paired with a correct cue word (in 50% of trials), or a new distractor word (from List 4 in Payne, Tucker [15]). They had to determine whether the word pair was in the list they had previously learned. Answer options were 'yes' or 'no'. The order of presentation was random, there was no time limit to give an answer, and participants were asked to be as accurate as possible. Every trial each answer was followed by a confidence rating. Participants had to indicate how confident they were their answer was correct. There were six options ranging from 'completely uncertain' to 'completely certain'. Participants were instructed that 'completely uncertain' meant that they answered completely based on guessing.

Figure 2. Schematic overview of study procedure and materials

Procedure and materials

1. **Informed consent + demographics questionnaire**
2. **Self-report metacognitive awareness inventory (MAI)**
3. **Memory task**
4. **Abstract reasoning task**



Note. MAI = Metacognitive Awareness Inventory.

Abstract Reasoning Task

The University of California Matrix Reasoning Task [UCMRT; 16] was administered via Qualtrics software (Qualtrics, Provo, UT). The UCMRT has previously been adapted for and validated on mobile platforms in a sample of healthy young adults [internal consistency based on Cronbach's α=.71; test-retest reliability based on Pearson's correlation coefficient: r=.62, p<.001; 16]. Participants were first presented with the practice trials as described in Pahor, Stavropoulos [16]. The task was UCMRT part A and consisted of 23 matrix-type problems for pattern completion with 8 answer options per trial. The decision was followed by a confidence rating in which participants had to indicate how confident they were their answer was correct. There were six options ranging from 'completely uncertain' to 'completely certain'. Participants were instructed that 'completely uncertain' meant that they answered completely based on guessing. There was no time limit for participants to respond and they were asked to be as accurate as possible. No feedback was given. There was no time limit for participants to respond and they were asked to be as accurate as possible.

Outcome Measures

Error recognition

Metacognitive Sensitivity. Whether a person can differentiate correct from incorrect responses answer was measured using the trial-by-trial confidence ratings and accuracy of the answers given. Metacognitive sensitivity was quantified with the type two area under the receiver operating characteristic curve (AUROC2) code from Fleming and Lau [12] in MATLAB (R2021b). Two metacognitive sensitivity scores were computed per person: one for the memory task and one for the abstract reasoning task. Scores can range from 0 to 1. A score of 0.5 is at chance and corresponds to no metacognitive sensitivity. A score above 0.5 indicates higher metacognitive sensitivity, with 1 representing perfect metacognitive sensitivity (people are high confident for correct trials, and low confident for incorrect trials). Scores below 0.5 are atypical but indicate reversed metacognitive sensitivity (people are high confident for incorrect trials, and low confident for correct trials).

Retrospective discrepancy. Discrepancy scores between the confidence judgments made after the tasks (ranging from 0 to 10) and performance accuracy (number of trials correct/total number of trials*10; ranging from 0 to 10) were calculated. Two retrospective discrepancy scores were calculated per person: one for the memory task and one for the abstract reasoning task. The discrepancy scores can range from -10 up to 10. Scores close to zero represent good metacognition and the further the score is away from zero (either negative or positive), the more this type of metacognition is impaired.

Metacognitive knowledge

Metacognitive Awareness Inventory (MAI). The knowledge of cognition subscale of the self-report questionnaire MAI consists of questions covering knowledge about self and about strategies, knowledge about how to use strategies, and knowledge about when and why to use strategies [8]. Scores on this subscale were calculated as mean scores of the items belonging to this subscale. Scores range from 0 (low) to 100 (high) level of perceived knowledge of cognition.

The regulation of cognition subscale of the self-report questionnaire MAI consists of questions covering the control aspect of learning: planning, information management strategies, comprehension monitoring, debugging strategies, and evaluation [8]. Scores on this subscale were calculated as mean scores of the items belonging to this subscale. Scores range from 0 (low) to 100 (high) level of perceived regulation of cognition.

Anticipation of performance

Prospective discrepancy. Discrepancy scores between the confidence judgments made before the tasks (ranging from 0 to 10) and performance accuracy (number of trials correct/total number of trials*10; ranging from 0 to 10) were calculated. Two prospective discrepancy scores were calculated per person: one for the memory task and one for the abstract reasoning task. The discrepancy scores can range from -10 up to 10. Scores close to zero represent good metacognition and the further the score is away from zero (either negative or positive), the more this type of metacognition is impaired. Negative scores represent under-confidence and positive scores represent over-confidence.

Data analysis

Statistical analyses were conducted with IBM SPSS Statistics version 27 for Windows. Reliability of the MAI subscales was measured using Cronbach's alpha (α). Reliability of the memory and abstract reasoning tasks was measured with odd-even split-half correlation (*r*) corrected with the Spearman-Brown formula. Descriptive analyses were performed to identify the distribution of scores on the different metacognitive measures. Multiple regression analyses were conducted to investigate whether scores on the questionnaires and accuracy of confidence judgments could predict metacognitive sensitivity (AUROC2). For these analyses, the prospective and retrospective discrepancy scores were transformed into absolute values (because both positive and negative values indicate poor metacognition). Thus, for the correlation analyses discrepancy scores range from 0 to 10. The raw data is available at https://doi.org/10.34894/U1YTW8. The experiment was not preregistered.

Results

Of the 165 participants that fit all inclusion criteria and entered the study, nine participants were excluded because they had invalid answers, five failed the validity check, and 23 did not finish all parts of the study (final sample N=128). As can be seen in Table 1, performance accuracy on the memory task (M=8.2, SD=1.2) was higher than on the abstract reasoning task (M=6.1, SD=2.1). Based on these accuracy scores, for both correct and incorrect trials, the metacognitive sensitivity was calculated using the AUROC2 (Figure 3). There is a large spread in metacognitive sensitivity scores. For the memory task, the AUROC2 is mostly above 0.5, indicating good metacognitive sensitivity. However, for the abstract reasoning task, many scores are around or below 0.5, indicating that this might not be a reliable measure for this task. A visual representation of the different metacognitive measures is presented in Figure 4.

Table 1. Accuracy scores on the cognitive tasks.

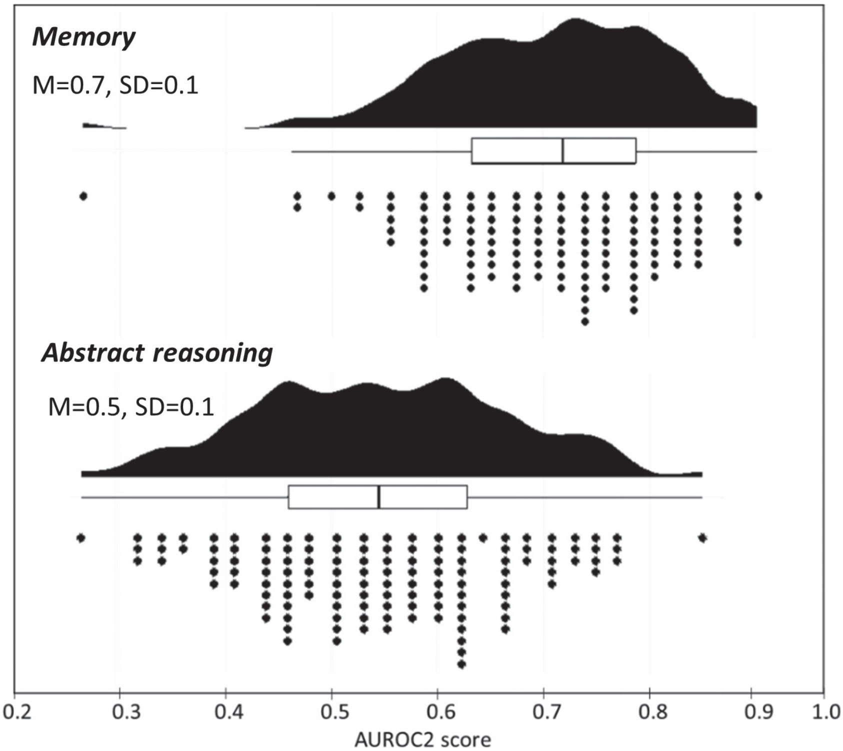
N=128	Mean (±SD)	Min – max
Memory task		
Accuracy (out of 10)	8.2 (±1.2)	3.8 – 10
Prospective confidence rating (out of 10)	5.6 (±1.6)	0.0 – 9.0
Retrospective confidence rating (out of 10)	6.1 (±2.0)	1.0 – 10.0
Mean confidence on trial-by-trial ratings (out of 6)	4.4 (±0.8)	2.4 – 6.0
Abstract reasoning task	**Mean (±SD)**	**Min – max**
Accuracy (out of 10)	6.1 (±2.1)	0.0 – 10.0
Prospective confidence rating (out of 10)	5.4 (±1.9)	0.0 – 9.0
Retrospective confidence rating (out of 10)	5.5 (±2.2)	0.0 – 9.0
Mean confidence on trial-by-trial ratings (out of 6)	4.2 (±0.8)	1.7 – 5.6

On both MAI questionnaire subscales, knowledge of cognition and regulation of cognition, participants indicated they were rather confident in their metacognitive capacities, as indicated by a score higher than 50. For both tasks, most people underestimated their performance as indicated by prospective and retrospective discrepancy scores below zero.

Reliability

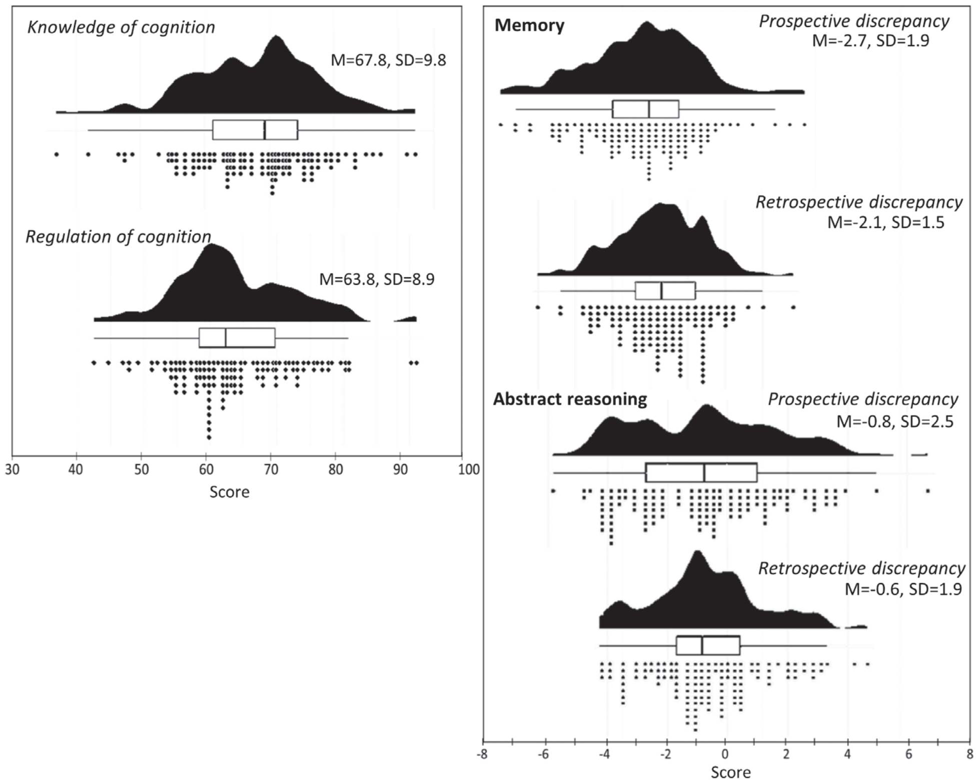
All measures showed high reliability scores. Cronbach's alpha was α=.827 on the MAI knowledge of cognition subscale and α=.859 on the regulation of cognition subscale. Odd-even split-half correlation analyses showed high reliability on the memory task (*r*=.828 for accuracy; *r*=.935 for confidence ratings) and on the abstract reasoning task (*r*=.843 for accuracy; *r*=.862 for confidence ratings).

Figure 3. ***Distribution of metacognitive sensitivity scores***



Note. The raincloud plots visualize the raw data and show the distribution of the dataset. The boxplots show medians and quartiles. The dots are the raw data points. AUROC2 = type two area under the receiver operating characteristic curve.

Figure 4. Distribution of metacognitive knowledge scores and of pro- and retrospective discrepancy scores.



Note. The raincloud plots visualize the raw data and show the distribution of the dataset. The boxplots show medians and quartiles. The dots are the raw data points.

Multiple Regression Analyses

Table 2 shows the multiple regression models predicting metacognitive sensitivity. For the memory task, this model significantly predicted metacognitive sensitivity ($F_{(4,123)}$=2.637, p<.05,R^2=.079). Significant predictors were higher prospective discrepancy scores (β=.233, p=.014) and lower retrospective discrepancy scores (β=-.185, p=.038). MAI knowledge of cognition and regulation of cognition subscales did not significantly predict metacognitive sensitivity (all p >. 703). For the abstract reasoning task, the model did not significantly predict metacognitive sensitivity ($F_{(4,123)}$=1.086, p=.366, R^2=.034) and none of the variables were significantly associated with metacognitive sensitivity.

Table 2. Multiple regression analyses predicting metacognitive sensitivity.

Dependent variable	Independent variables	R2	Adjusted R2	Standardized beta	*p*-value
Memory task		.079	.049		
Metacognitive sensitivity (AUROC2)	Knowledge of cognition (MAI)			.046	.703
	Regulation of cognition (MAI)			<.001	1.000
	Prospective discrepancy score (absolute values)			.223	**.014**
	Retrospective discrepancy score (absolute values)			-.185	**.038**
Abstract reasoning task		.034	.003		
Metacognitive sensitivity (AUROC2)	Knowledge of cognition (MAI)			-.098	.407
	Regulation of cognition (MAI)			.107	.365
	Prospective discrepancy score (absolute values)			.173	.071
	Retrospective discrepancy score (absolute values)			-.100	.295

Note. AUROC2 = type two area under the receiver operating characteristic curve. MAI = Metacognitive Awareness Inventory.

Discussion

The aim of this study was to explore how metacognitive knowledge, anticipation and evaluation of performance predict metacognitive sensitivity. The results show that in this healthy population there is large variability of scores on all the different metacognitive measures. There is a wide range of scores on all measures; some people score quite low while others score quite high. Furthermore, metacognitive sensitivity on the memory task was predicted by poor anticipation of performance (large prospective discrepancy score) and good retrospective evaluation of performance (small retrospective discrepancy score). This was not the case for the abstract reasoning task. Moreover, metacognitive knowledge was not a significant predictor of metacognitive sensitivity in both tasks, supporting the notion that the two measures assess metacognition at a different level. The questionnaire items cover a broad range of metacognitive behaviors and strategies, they relate to situations more distant in time, and might be more abstract than the in-the-moment confidence judgments after every trial. This confirms the idea that metacognition can be split into metacognitive knowledge and online awareness as described in different models [e.g. 1, 6].

The hypothesis that there would be a negative association between metacognitive sensitivity and discrepancy scores was true for the retrospective discrepancy score but not the prospective discrepancy score, and only in the memory task. In the memory task, higher metacognitive sensitivity during the task was associated with more accurate judgment of performance after the task. This suggests that people use the metacognitive information during the task to shape their evaluation after the task, as has been suggested in previous research [18]. The shift from a positive correlation between metacognitive sensitivity and prospective discrepancy to a negative correlation with retrospective discrepancy supports this idea. The confidence judgment after the task is different from before the task, and this might be due to metacognitive experiences during the task such as familiarity, difficulty, satisfaction, and effort [19]. The regression model for the memory task was significant but explained only a small proportion of variance. This indicates that there are likely other important predictors for metacognitive sensitivity, such as domain-specific self-concept [20].

Perhaps no significant associations between the metacognitive measures were found in the abstract reasoning task because there was not enough metacognitive information to be gained during the task. Mean metacognitive sensitivity in the abstract reasoning task was at chance level, indicating that it was difficult for participants to correctly distinguish their correct from incorrect responses. This information can then also not shape the evaluation after the task. In future research, it would be interesting to investigate the underlying mechanisms of how prospective and retrospective confidence judgements are formed. This could be done by having more elaborate prospective and retrospective confidence ratings, such as the Metacognitive Experiences Questionnaire [21]. Moreover, it is important to adopt a task that is not too easy because people need to have both correct and incorrect trials, but also not too difficult because people need to know to some degree whether their answer was correct or not. A solution could be to use an adaptive task.

The strengths of this study are the large sample size, and the inclusion of different measures of metacognition, which allows for a proper investigation of the associations between the different elements of metacognition. However, there are also some limitations to this study. The first is that the study was fully online, making it difficult to check whether people took part seriously or whether they took long breaks. When replicating this study in a more controlled environment such as a lab, this can be registered. For now, we attempted to control for this by adding validity questions. These questions led to exclusion of five participants who indicated they 'just clicked through' the study. Furthermore, in replication studies the tasks should be counterbalanced or randomized to control for practice effects or fatigue. Secondly, the included sample was very homogenous, including mostly highly educated healthy people within a small age range. This limits generalizability of the results. Thirdly, the metacognitive sensitivity measure (AUROC2) might not be very meaningful when there is a floor or ceiling effect in performance accuracy. There must be enough correct and incorrect trials for people to be able to distinguish the two types of trials with their confidence judgment. Similarly, if the task is too difficult and people do not know whether their answer is correct or incorrect, it is difficult to give a confidence judgement. This also argues for the use of an adaptive task in future studies. The current study was a behavioral study. However, for a more comprehensive understanding of metacognition, it would be interesting to investigate which brain areas or networks are involved in the different elements of metacognition.

The current study shows that task-specific online measures of metacognition can predict metacognitive sensitivity, but more general measures of metacognition cannot. Moreover, it provides a framework to investigate the associations between different elements of metacognition within persons. An interesting application of this paradigm would be to investigate these associations in populations with metacognitive impairments, such as after brain disorders. This could give an indication of where the problem arises and, possibly, what should be targeted to improve metacognition.

Statements and Declarations

Conflict of interest: none.

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CHAPTER 3

Neural Correlates of Metacognitive Sensitivity for Recognition Memory

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Submitted

CHAPTER 4

Neural Correlates of Impaired Self-awareness of Deficits after Acquired Brain Injury: A Systematic Review

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Abstract

Self-awareness is essential for the process and outcome of rehabilitation but is often affected by acquired brain injury (ABI). While many studies investigated the psychological aspects of self-awareness deficits, the biological underpinnings are not well understood. The aim of this systematic review was to identify the neural correlates of self-awareness after ABI. Results indicate that anticipation of future problems is associated with lesions and decreased neural functioning in the right frontal lobe, as well as increased diffusivity throughout the white matter of the brain. Poor behavioral adjustment on implicit awareness tasks is associated with less functional connectivity of anterior cingulate cortex and right/middle inferior frontal gyri to the fronto-parietal control network, as well as more activation in the left insula and left parietal operculum during error processing. Recognition of mistakes is associated with internetwork connectivity of anterior/posterior default mode network to salience network. In conclusion, after ABI, different results in brain activation and connectivity are found depending on level of awareness measured. Future studies are necessary to confirm these findings.

Introduction

Acquired brain injury (ABI), such as stroke or traumatic brain injury (TBI), is one of the major causes of disability worldwide [1]. People with severe ABI often suffer from a range of cognitive and behavioral deficits for which rehabilitation treatment is necessary [2]. Unfortunately, the rehabilitation process is hindered when people exhibit reduced self-awareness of their deficits [3]. An impairment in self-awareness after ABI is associated with decreased motivation for and participation in therapy [4]. Consequently, worse psychosocial rehabilitation outcomes are found, such as difficulties in societal participation, relationships, and return to work [5]. Therefore, self-awareness is an essential target of rehabilitation that requires attention, but is often considered a limiting factor in treatment success.

The exact cause of impaired self-awareness of deficits after ABI is unclear but most researchers and clinicians assume it is a combination of psychological factors and changes in brain functioning [6]. Despite that, literature to date has primarily focused on the psychological aspects, such as denial of changes in functioning, anxiety, defensiveness, and a variety of coping behaviors. Studies examining the neural correlates of self-awareness remain scarce, possibly due to the complexity of the topic or trouble recognizing it in clinical practice. However, understanding the neural aspects of self-awareness of deficits after ABI is necessary for the development of more comprehensive theoretical models of self-awareness. This, in turn, can contribute to the development of more effective measurement instruments, targeted interventions, and understanding limitations in current approaches of the problem.

One of the first influential models relating brain systems to self-awareness was presented by Stuss [7] in which different types of self-awareness were categorized in a hierarchy. The lowest level of self-awareness is the actual knowledge and recognition of a deficit by the affected person. Lacking knowledge of a deficit often occurs in routinized behavior, such as speech. For example, patients with Wernicke's aphasia (impairment of speech comprehension) might not be able to monitor and, thus, might not be aware of the nonsensical speech they produce. The next level is the integration of this knowledge into adaptive behavior. This executive control of novel or goal-directed behavior is regulated by the frontal lobes. Deficits at this level lead to impaired judgment or disorganized use of knowledge of a deficit. For example, one might be aware of memory problems but fail to adjust behavior accordingly, such as using a compensation strategy like a diary. At the highest level, the knowledge and executive control of a deficit is integrated into a timeframe. Memories and experiences of the past, perceptions and emotions of the present, and expectations of the future are used to create mental representations of the current self in the social environment. This is also regulated by the frontal lobes. With an impairment at this level of awareness, one might be unable to imagine that a deficit can lead to a problem in the future.

Since the introduction of this model, studies have consistently confirmed that behaviorally there are different types of self-awareness. Similar models have been created that isolate different aspects of self-awareness behavior. In general, this can be divided into online awareness of behavior during a specific task and offline awareness, which refers to reflecting on one's behavior before or after a task [8]. Similarly, efforts have been made to create optimal instruments to measure different self-awareness behaviors. Unfortunately, there is a gap in literature relating specific brain systems to these different levels of awareness, especially after ABI.

Empirical studies in non-ABI populations have confirmed the importance of the frontal lobes for self-awareness, but also suggest involvement of other brain regions from a neural network approach. For example, a study in individuals with neurodegenerative disease confirmed the role of frontal regions in cognitive self-awareness [9]. Similarly, the frontal lobes are of major importance for self-awareness in healthy individuals [10]. However, studies indicate that other brain regions are involved in self-awareness in healthy participants as well, such as cortical midline structures [10, 11]. Specifically, it has been suggested that the posterior cingulate cortex (PCC) is engaged when thinking about oneself and is influenced by the medial prefrontal cortex [mPFC; 12]. Over the years, several studies have been done on the neural correlates of self-awareness (deficits) after ABI as well, but there is no systematic overview of the findings yet.

There are various methods of assessment that can be used to differentiate between levels of self-awareness. A recent review classified the measurement instruments into three categories: (1) self-proxy discrepancy, (2) rating by clinician, and (3) performance-based discrepancy [8]. In the self-proxy discrepancy method, patients' self-ratings are compared to the rating of a significant other, caregiver, or therapist. This is often in questionnaire format and includes multiple domains. This requires judgments of one's performance and/or deficits as well as integrating this knowledge into a timeframe and, therefore, reflects the highest level of self-awareness. The rating by a clinician is often based on interviews, observed behavior, and test scores. This could reflect the second level of awareness because clinicians can observe when errors are made and whether behavior is adapted accordingly. The performance-based methods are often basic tasks within a certain domain. Depending on the task, these can reflect all levels of self-awareness. The lowest level can be measured when, after a task, participants are explicitly asked whether mistakes were recognized (referred to in this paper as explicit self-awareness). If the task requires behavioral changes after an error has been recognized, this reflects the second level of self-awareness. These tasks rely on the assumption that self-awareness is necessary to successfully complete the task. Hence, these will be categorized as implicit self-awareness methods. Tasks that require mental representations of the self measure the highest level of self-awareness. Such tasks could include estimating expected performance prior to a task, anticipating problems in future situations, as well as retrospective reflection on behavior. By classifying the methods of assessment this way, the neural correlates at each level of self-awareness can be investigated.

The aim of this systematic review is to identify the structural and functional neural correlates of the different levels of self-awareness of cognitive and behavioral deficits after ABI. More specifically, associations between MRI-measures and the different measurement methods of self-awareness were investigated. The results are considered in relation to theoretical models of self-awareness after brain injury. This information leads to a better understanding self-awareness of deficits after ABI and could, ultimately, result in new or better approaches to treatment in the clinic.

Methods

Study Selection

This systematic review was designed according to the guidelines of Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols [PRSIMA-P; 13]. Inclusion criteria were: (1) the study is published in English in a peer-reviewed journal; (2) the study is published during the 20 years before the search date, which was November 20th 2019; (3) the study population is human adults who are at least 18 years old (4) and were diagnosed with acquired brain injury such as stroke, TBI or hypoxia; (5) there has to be a direct measure of self-awareness, which can either be a self-proxy discrepancy score, performance-based discrepancy score, or a clinician-rated score; (6) structural and/or functional MRI had to be conducted as part of the study; and (7) the neuroimaging results have to relate certain brain areas or networks to self-awareness. Articles were excluded if they (1) included patients with neurodegenerative diseases (such as forms of dementia or Parkinson's disease) or mixed samples with less than 50% ABI patients; (2) were single-case studies; (3) only measured self-awareness of physical or motor deficits; or (4) only retrieved imaging data retrospectively from medical files and not specifically performed scans as part of the study. The rationale for excluding studies concerning self-awareness of physical or motor deficits is that levels of self-awareness can differ per domain of functioning. For example, self-awareness of cognitive and behavioral deficits is often more impaired than that of physical deficits. Moreover, impaired self-awareness of motor deficits have been found to be unrelated to impaired self-awareness of cognitive deficits [14, 15]. Given the complexity of impaired self-awareness and that the level of self-awareness can differ per domain, this paper focusses on self-awareness of cognitive and behavioral deficits, not that of physical deficits. The rationale for excluding scans derived from medical files was that the time between the initial scan, which is usually at emergency room admittance, and the self-awareness measurement for the study could be years, and brain structure and function could have changed in the meantime.

The databases Pubmed, PsycINFO, Web of Science and EMBASE were systematically searched for relevant literature on November 20th 2019. The full list of search terms can be found in appendix 1. Search terms were always terms relating to self-awareness combined with terms relating to imaging techniques and terms relating to brain injury. Titles of all potentially relevant studies were collected in Endnote X8.2. Duplicates were removed. After inspection of in- and exclusion criteria, titles were screened for eligibility by one author (AT). If there was doubt, the study was included. Relevant abstracts were uploaded and screened for eligibility in Covidence by two authors (AT and CQ). Any disagreements were discussed and resolved. If in- or exclusion was unclear based on the abstract, full texts were assessed. Reference lists of included articles were checked for further relevant articles.

Classification, Data Collection, and Synthesis

The included studies were first classified according to method of self-awareness assessment: self-proxy discrepancy, rating by clinician, or performance-based discrepancy [8]. A second classification was made based on imaging technique: structural imaging studies were separated from functional imaging studies.

Variables extracted from the studies included demographical factors such as sample size, age, sex, education, time since injury, type of injury, and injury severity. Data gathered on self-awareness assessment included measurement technique, awareness score, and interpretation of that score. Additionally, information on imaging procedure, imaging technique, and task contrast was extracted. If relevant, the task used during imaging was noted. The imaging results and interpretations of which brain areas are involved in self-awareness were also extracted from the papers. The relevant data was extracted from the studies by two authors independently (AT and CQ). This was then compared and any discrepancies were resolved together by referring back to the paper. The principal measures for this review were results relating self-awareness of deficits to structural and functional neural correlates. Brain areas involved in self-awareness of deficits and directions of correlations were summarized and interpreted in relation to methodological differences such as type of self-awareness and imaging technique.

Quality Assessment

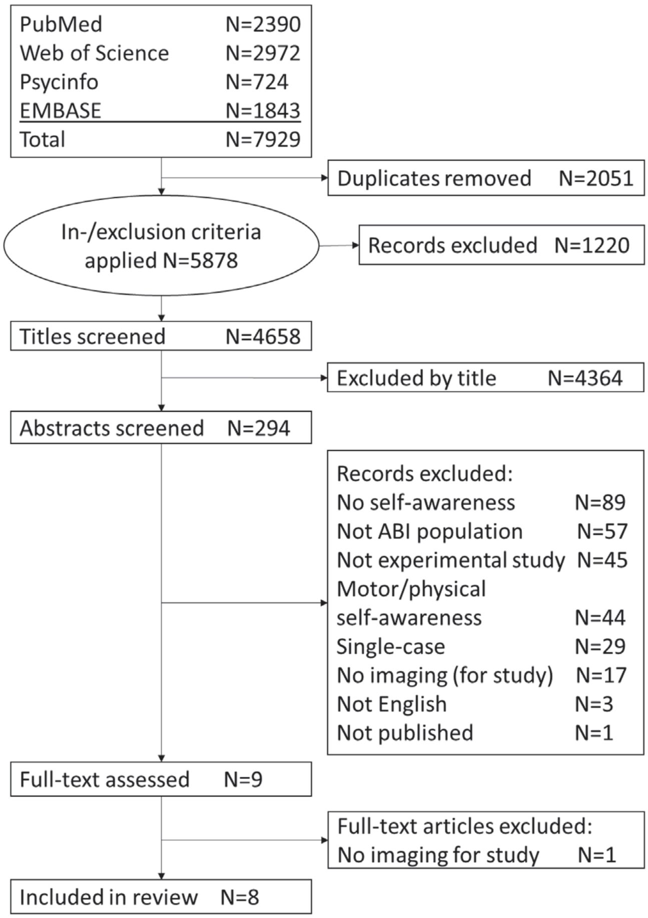
Quality of the included studies was assessed by two authors (AT and CQ; see figure 2). Quality of the studies was evaluated based on the nine criteria described in Wolters, van de Weijer [16]: (1) description of participants; (2a) description of imaging procedure and instructions; (2b) description of self-awareness measure; (3) description of imaging analysis; (4) specification of regions of interest; (5) reproducibility; (6) statistical testing; (7) multiple testing problem; (8) figures and tables; and (9) quality control measures. Criteria 2a and 2b were specified in the current study to ensure that the self-awareness measure as well as the imaging procedure were well described. Each criterion could be scored with 1 point (+), 0.5 points (±), or 0 points (-). Total score was calculated and corrected for number of applicable criteria (total score/number of applicable criteria*10). A score of 7.5 or higher was considered as good quality, a score between 4 and 7.5 as fair quality, and a score of 4 or less as poor quality [16]. Quality of papers is considered while interpreting and discussing the results of the data synthesis. The full assessment tables per study can be found in the supplementary material.

Results

Search Results and Classification

The flowchart of the selection procedure can be found in figure 1. After title screening (N=4658) and abstract screening (N=294), nine full texts were assessed of which eight were included in the review. Three studies used self-proxy discrepancy scores to measure self-awareness [17-19], three studies used performance-based discrepancy scores [20-22], and two studies included both self-proxy discrepancy scores as well as performance-based discrepancy scores [23, 24]. There were no studies in which a rating by a clinician was used to measure self-awareness. Study characteristics can be found in table 1.

Figure 1. Flowchart of selection procedure.



Self-proxy Discrepancy Method

As can be seen in figure 2, one paper that used self-proxy discrepancy scores to measure self-awareness was of poor quality [18], one of fair quality [17], and three papers were of good quality [19, 23, 24]. The self-proxy discrepancy score in the study by Ham, Bonnelle [24] was merely used to confirm self-awareness levels of the groups. These results were not directly associated to neuroimaging findings and, thus, will not be further discussed in this section.

All four studies used different questionnaires to measure self-awareness, including the Barthel Index [17], Awareness Questionnaire [18], Dysexecutive Questionnaire [19], and Patient Competency Rating Scale [23]. In these questionnaires, people estimate how well or poorly they will be able to perform specific daily life activities in the near future and, thus, require mental representations of the self in the environment. The proxies who filled in the questionnaires were either patients' primary caregivers [17] or relatives [18, 19, 23]. Self-awareness scores were calculated as the difference in total score between the patient and the primary caregiver or relative. Higher discrepancy scores represent poorer self-awareness. Behavioral results showed that certain ABI groups overestimated their functioning [17, 23] and underestimated their deficits [19].

Structural Neural Correlates of Self-Awareness Based on Self-proxy Discrepancies

Structural MRI or CT scans were used to determine lesion location [17, 18], injury severity [23], and white matter abnormalities [19]. Results are depicted in figure 3. When comparing TBI patients with impaired self-awareness to patients with adequate self-awareness, the distribution of lesions showed that those with impaired self-awareness had significantly more frontal lesions (shaded area 1 in figure 3; chi-square=8.97; $p<0.01$), but there were no differences with regard to diffuse or posterior cortical lesions [18]. Comparing patients with right to left hemisphere cerebrovascular lesions, it was found that the self-proxy discrepancy score was significantly larger in those with right hemisphere lesions (shaded area 2 in figure 3; Mann–Whitney test; $p<0.0001$), indicating more impaired self-awareness [17]. The other two studies correlated patients' structural neuroimaging findings to the self-proxy discrepancy scores on the self-awareness measures. An almost significant positive correlation ($r=0.44$; $p=0.055$) was found between impaired self-awareness and right frontal lobe gray and white matter damage (shaded area 3a in figure 3), whereas this correlation was much weaker ($r=0.29$; $p=0.22$) in TBI patients with left frontal lobe damage [23]. Furthermore, mean diffusivity in the whole white matter of TBI patients positively correlated with impaired self-awareness [area 4 in figure 3; $r=0.26$; p=not reported; 19].

Table 1. Characteristics of studies measuring neural correlates of self-awareness of cognitive deficits in acquired brain injury.

Study (year)	Sample size (N)		♂/♀		Age in years mean (SD)		Injury Time1	Injury severity2	Self-awareness			Imaging		
	ABI	HC	ABI	HC	ABI	HC	mean (SD)		Method3	Measure	Findings	Technique	Contrast	Significant findings
Tezuka et al. (2013)	31 LHD stroke		10/20		79.1 (8.5)[a]		≥ 3			BI patient - relative	Overestimation of activities daily living in RHD	Structural: CT or MRI	Left hemisphere damage (LHD) vs. Right hemisphere damage (RHD)	RHD associated with impaired self-awareness
	30 RHD stroke		10/21		80.7 (8.8)[a]		≥ 3							
Bivona et al. (2014)	14 TBI-ISA	28	12/2	21/7	37.2 (13.3)	34.5 (9.9)	27.3 (25.4)[4]	S	S-P	AQ patient - relative	Median split to make groups	Structural: CT or MRI	Impaired (ISA) vs adequate (ASA) self-awareness	Damage in frontal cortical regions ISA > ASA No difference in axonal injury or posterior cortical regions
	14 TBIASA		9/5		30.6 (8.9)		25.7 (20.6)[4]							
Lesimple et al. (2019)	63 TBI		55/8		39.7 (15.0)		63.4 (20.7)	S	S-P	DEX relative -patient	Underestimation of deficits	Structural: MRI, DWI	Within TBI: correlations white matter measures and self-awareness	Diffusivity in whole white matter negatively associated with self-awareness
Schmitz et al. (2006)	20 TBI	20	13/7	8/12	27.1 (10.8)	28.1 (11.4)	2.7 (0.6)[4]	M	S-P	PCRS patient - relative	Overestimation of performance	Structural: MRI	Left frontal (LFD) vs right frontal (RFD) damage correlations with self-awareness	RFD positively correlated with impaired self-awareness
									PB	Self-evaluation task	Equal performance for TBI and HC	Functional: task fMRI	TBI vs HC: activation during self-evaluation task vs word valence task: within + between groups.	TBI > HC: anterior cingulate cortex, precuneus and right anterior temporal pole
													Within TBI: self-evaluation activation regressed with predictor PCRS discrepancy	Right superior frontal gyrus functioning associated with self-awareness
Ham et al. (2014)	63 TBI	24	46/17	16/8	38.0 (12)	36.2 (10.2)	29 (74)	M/S	S-P	FrSBe patient - relative	Underestimation of deficits in ISA	Structural: MRI, DTI	ISA vs ASA vs HC: measures of white matter within fronto-parietal control network (FPCN)	No differences
	23 ISA	13/10	39.4 (12.8)	46.9 (115.3)										
	40 ASA		33/7		37.3 (11.6)		19.7 (30.1)							
Subset	48 TBI	25	37/11	17/7	35.7 (10.9)	34.8 (9.6)			PB	Stop-change task	Lower performance monitoring in ISA	Functional: rest fMRI	ISA vs ASA vs HC: functional connectivity whole brain + ROI nodes of FPCN	ISA reduced connectivity FPCN to dorsal anterior cingulate cortex, right middle frontal gyrus and right inferior frontal gyrus

Table 1. Continued

Study (year)	Sample size (N)		♂/♀		Age in years mean (SD)		Injury Time1	Injury severity2	Self-awareness			Imaging		
	ABI	HC	ABI	HC	ABI	HC	mean (SD)		Method3	Measure	Findings	Technique	Contrast	Significant findings
	18 ISA		NR		NR		NR							
	30 ASA		NR		NR		NR							
												task fMRI	ISA vs ASA vs HC: functional connectivity during error processing + response inhibition	ISA > ASA: left insula and left parietal operculum
Grossner et al. (2018)	34 TBI	28	19/15	16/12	33.4 (13.1)	34.1 (12.6)	51.7 (85)	S	PB	Reasoning task	Equal performance for TBI and HC	Structural: MRI	TBI vs HC: gray matter volume whole brain + ROI frontal, temporal and occipital regions; and correlations with self-awareness	HC positive association between metacognitive accuracy and left posterior, left orbital and left dorsolateral regions; TBI no association
Grossner et al. (2019) *Partly overlaps with 2018 study*	21 TBI	23	12/9	12/11	32.9 (14.0)	36.9 (12.1)	49.9 (77.0)	S	PB	Reasoning task	Equal performance for TBI and HC	Functional: rest fMRI	TBI vs HC: whole brain network metrics; network connectivity within and between ROI subsystems[5]	TBI self-awareness positively associated with connectivity between anterior DMN and salience network; and between posterior DMN and salience network (opposite correlations for controls)
Garcia-cordero et al. (2019)	15 stroke	19	7/8	8/11	61.87 (6.7)	67.8 (7.8)	> 6	NR	PB	Visual perception task	Less implicit monitoring in FIS than HC	Structural: MRI	Within fronto-insular stroke (FIS): whole brain voxel-based lesion-symptom mapping	Ventromedial frontal damage positively associated with explicit awareness Fronto-temporo-insular damage positively associated with implicit awareness

[1]Injury time=time since injury in month; [2]Injury severity: S=severe, M=moderate; [3]Self-awareness assessment method: S-P=self-proxy discrepancy, PB=performance based; [4]not reported but calculated based on the paper; [5]subsystems were: anterior DMN network (middle frontal, superior frontal); posterior DMN network (posterior cingulate, precuneus, temporal pole); attention network (middle temporal, lateral occipital, ventral frontal); salience network (insular cortex, anterior cingulate); frontoparietal network (precentral gyrus, superior parietal, lateral prefrontal); 'residual' network (sensory-motor, auditory, visual). ABI=acquired brain injury; ASA=adequate self-awareness; AQ: Awareness questionnaire; BI= Barthel Index; CT=computed tomography; DEX= Dysexecutive questionnaire; DMN=default mode network; DTI=diffusion tensor imaging; DWI=diffusion weighted images; (f)MRI=(functional) magnetic resonance imaging; FrSBe=Frontal Systems Behaviour questionnaire; FPCN=fronto-parietal control network; ROI=region of interest; HC=healthy controls; ISA=impaired self-awareness; LHD=left hemisphere damage; NR=not reported; PCRS=Patient competency rating scale; RHD=right hemisphere damage; TBI=traumatic brain injury.

Figure 2. Quality assessment scores per study.

Note. Based on nine criteria described in Wolters, van de Weijer [16]. Each criterion could be scored with 1 point (+), 0.5 points (+/-) or 0 points (-). Total score was calculated based on number of applicable criteria. A score of 7.5 or higher was considered as good quality (green), 4-7.5 as fair quality (orange) and 4 or less as poor quality (red).

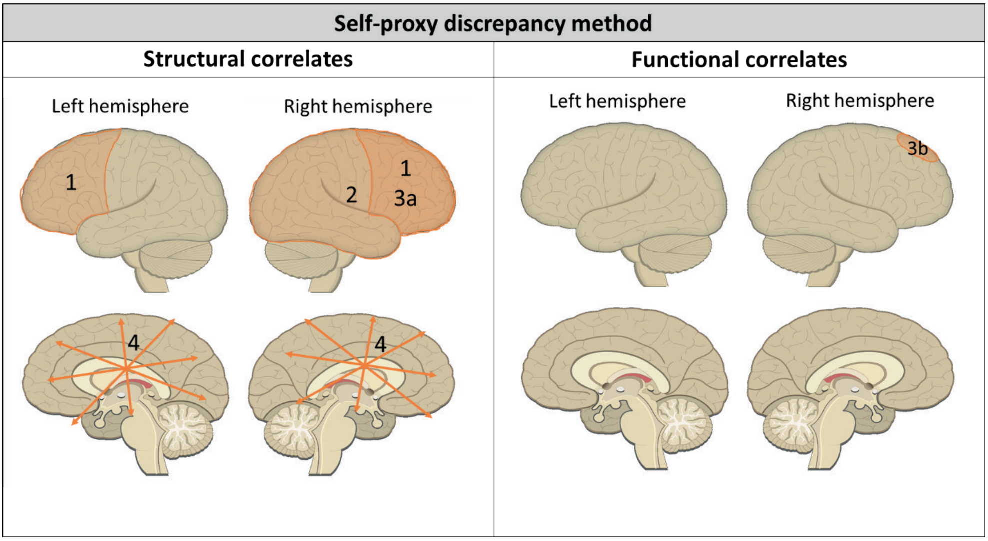
Functional Neural Correlates of Self-Awareness Based on Self-proxy Discrepancies

One study used the self-proxy discrepancy score to predict brain activation during a self-evaluation task [23]. In the task, TBI patients had to rate trait adjectives as relating to themselves or objectively rate whether the valence of the trait adjective was positive or not. Brain activity was compared between these two conditions, and the difference was attributed to self-awareness. Subsequently, it was investigated whether PCRS discrepancy scores were predictive of the self-awareness-related brain activation seen during the task. Higher self-proxy discrepancy scores (indicating less self-awareness) were associated with less BOLD signal difference between conditions in the right superior frontal gyrus (SFG) during the self-awareness task [shaded area 3b in figure 3; r=-0.26; p=0.005; 23]. This correlation was not significant in the left SFG [r=-0.23; p=0.16; 23].

Summary Self-proxy Discrepancy Method

The four studies above suggest that impaired self-awareness after ABI, as measured by self-proxy discrepancy scores, is associated with lesions, white and gray matter damage, and decreased task-related activation in the right frontal lobe, as well as higher mean diffusivity in the whole white matter. In the study by Tezuka, Meguro [17], participants are stroke patients, there is a larger proportion female participants than male participants, mean age is around 80 years old, and injury severity is not reported. The three other studies included TBI patients, have a larger proportion of male participants, mean age ranges from 27.1 to 39.7 years old, and injury severities are moderate to severe. In light of these differences, the results reported by Tezuka, Meguro [17] might be less comparable to the others. Results of Bivona, Riccio [18] and Lesimple, Caron [19] should be interpreted with caution since they did not correct for multiple testing. Nevertheless, the overall conclusion remains that right frontal brain areas and white matter diffusivity throughout the brain are involved in impaired self-awareness after ABI when measured by self-proxy discrepancy scores.

Figure 3. Structural and functional neural correlates of impaired self-awareness as measured with self-proxy discrepancy scores after ABI.



Note. **1.** Lesions in frontal cortical areas associated with impaired self-awareness [18]. **2**. Right hemisphere lesions associated with impaired self-awareness [17]. **3a**. Right frontal lobe gray and white matter damage associated with impaired self-awareness. **3b.** Less BOLD activation in right superior frontal gyrus during self-evaluation task associated with impaired self-awareness [23]. **4.** Higher mean diffusivity in the whole white matter associated with impaired self-awareness [19].

Performance-Based Discrepancy Method

All of the studies measuring self-awareness by means of a performance-based discrepancy method were of good quality, as can be seen in figure 2 [20-24]. For the purpose of this review, the methods are split into explicit self-awareness methods and implicit self-awareness methods. In explicit self-awareness methods, the participants are consciously triggered to evaluate their performance, while in implicit self-awareness methods they are not.

Implicit Self-Awareness. Using a simple perceptual task in which participants had to select the largest circle on the screen, Garcia-Cordero and collegues [21] asked stroke patients whether they wanted to stick with their answer and risk winning or losing three points, or go for the safe option to opt out and receive one point. Self-awareness in this task is related to the second level of awareness, adapting behavior. Namely, implicit performance monitoring was the fraction of times participants would take the risk out of the total number of these types of trials. Stroke patients showed significantly less implicit monitoring than healthy controls in this risk-taking task [21]. Another study assessed implicit self-awareness during a stop-signal task, which allows dissociation of error processing and response inhibition [24]. This task also measures self-awareness on the level of behavioral change. Accuracy on the stop-signal task was the same when comparing an impaired self-awareness TBI group to an adequate self-awareness TBI group and healthy control group on the stop-signal task [24]. However, the impaired self-awareness group was generally slower to respond, had greater intra-individual variability, and showed greater post-error slowing [24].

Explicit Self-Awareness. Explicit self-awareness was assessed using behavioral tasks in combination with a confidence judgment after each trial. These tasks require recognition of errors, reflecting the first level of awareness. In the perceptual task used by Garcia-Cordero, Sedeno [21], participants were asked to report confidence of their answer on a slider ranging from low confidence to high confidence. The mean of these values was used as a measure of explicit monitoring. Stroke patients did not significantly differ from controls regarding confidence [21]. Another study, described in two papers, used an adapted version of the Matrix reasoning task in which participants had to select an image to complete a pattern. After each trial, they were asked to rate how confident they were of their answer, ranging from completely certain to completely uncertain on a 6-point Likert scale [20, 22]. Self-awareness was measured as metacognitive accuracy and calculated using the area under a receiver operating characteristic (AUROC) curve. Behavioral results indicate that TBI patients did not differ from healthy controls in levels of explicit self-awareness [20]. Finally, Schmitz et al. [23] used a task in which participants had to rate trait adjectives as relating to themselves or objectively rate whether the valence of the trait adjective was positive or not. Brain activity was compared between these two conditions, and the difference was attributed to self-awareness. This task requires mental representations of the self, reflecting the highest level of awareness. Results show no significant behavioral difference between TBI patients and healthy controls [23].

Structural Neural Correlates of Self-Awareness Based on Performance-Based Discrepancies

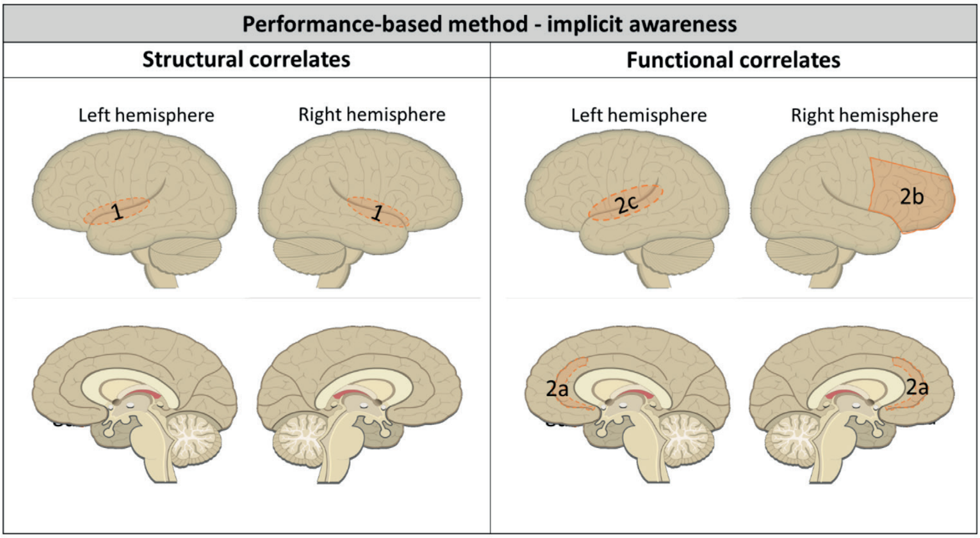
Implicit Self-Awareness. Results are visualized in figure 4. Voxel-based lesion symptom mapping was used to identify which lesion locations correlated with implicit and explicit awareness in stroke patients [21]. For implicit self-awareness, a positive association was found between lesions in fronto-temporo-insular brain areas and impaired implicit awareness [shaded area 1 in figure 4; t-score>1.82, $p<0.05$, FDR-corrected; 21]. Another study compared focal lesion location and volume between adequate and impaired TBI patient groups using lesion overlap images. However, formal statistical analysis was not possible due to a lack of common lesions, indicating no obvious relationship [24]. In the same study structural connectivity of the dorsal anterior cingulate cortex (ACC) to bilateral insulae (tracts of fronto-parietal control network; FPCN) was assessed using diffusion tensor imaging (DTI), comparing a group of TBI patients with impaired self-awareness to a group of TBI patients with adequate self-awareness and a control group [24]. Likewise, no significant differences were found between the brain-injured groups regarding fractional anisotropy values in this tract [24].

Explicit Self-Awareness. A depiction of the results can be found in figure 5. Voxel-based lesion symptom mapping showed positive associations between ventromedial lesions and confidence (shaded area 1 in figure 5; t-score>2.88, $p<0.05$, FDR-corrected), which was used as measure of explicit self-awareness [21]. Another study showed that in a healthy control group, better explicit self-awareness was associated with more gray matter volume in the left posterior region (shaded area 2a in figure 5; PCC, angular gyrus, and supramarginal gyrus), the left orbital region (shaded area 2b in figure 5; orbital gyrus and orbital H-shaped sulcus), and the left dorsolateral region [shaded area 2c in figure 5; superior frontal gyrus, middle frontal gyrus, and middle frontal sulcus; 20]. Remarkably, these associations were absent in the brain-injured population, where self-awareness was not significantly associated with total or regional gray matter volume [20]. However, total gray matter volume was lower in the TBI group. Moreover, gray matter volume in the right hemisphere was not significantly associated with self-awareness in either group in this study [20].

Functional Neural Correlates of Self-Awareness Based on Performance-Based Discrepancies

Implicit Self-Awareness. A summary of the results can be found in figure 4. Functional connectivity within the FPCN was compared between a group of TBI patients with impaired self-awareness and one with adequate self-awareness [24]. The FPCN in this study included dorsal ACC, bilateral insulae, bilateral temporo-parietal junctions, and bilateral middle and inferior frontal gyri. Results show that in resting state, the impaired self-awareness TBI group showed significantly less functional connectivity of the dorsal ACC (shaded area 2a in figure 4), right inferior frontal gyrus and right middle frontal gyrus (shaded area 2b in figure 4) to the rest of the FPCN [24]. Additionally, brain activation during a stop-signal task was compared between these groups. During error processing, the impaired self-awareness TBI group showed increased activation in the left insula and left parietal operculum [shaded area 2c in figure 4; 24]. Brain activation after successful response inhibition was similar in adequate and impaired self-awareness groups [24].

Figure 4. Structural and functional neural correlates of impaired implicit self-awareness as measured with performance-based discrepancy scores after ABI.



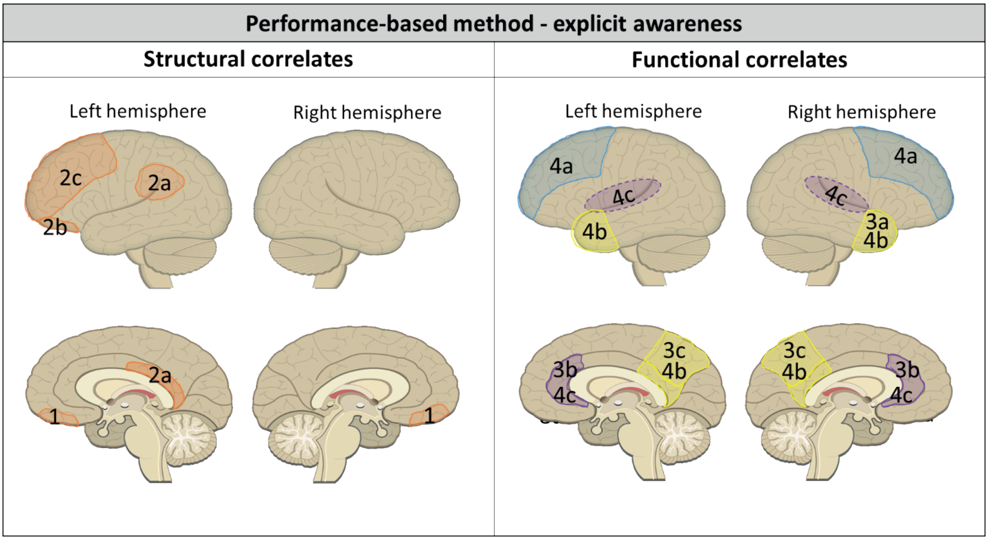
Note. **1.** Fronto-temporo-insular lesions associated with impaired implicit self-awareness [21]. **2.** Less functional connectivity of the **2a.** dorsal anterior cingulate cortex and **2b.** right middle and inferior frontal gyri to the rest of the FPCN in resting state associated with impaired implicit self-awareness. **2c.** Increased activation in left insula and left parietal operculum during error processing (stop-signal task) associated with impaired implicit self-awareness [24].

Explicit Self-Awareness. Results are shown in figure 5. During a self-evaluation task (when participants were relating adjectives to themselves as opposed to objectively rating their valence) TBI patients and healthy controls both showed activation in midline cortical structures [23]. However, compared to healthy controls the TBI group showed significantly more activation in the right anterior temporal pole [shaded area 3a in figure 5; maxima t=4.12, d.f.=19, p uncorrected <0.001; 23], ACC (shaded area 3b in figure 5; maxima t=4.72, d.f.=19, p uncorrected <0.001), and precuneus (shaded area 3c in figure 5; maxima t=3.68, d.f.=9, p uncorrected <0.001). In another study, resting state functional connectivity between and within brain networks including the attention network, default mode network (DMN), salience network, and frontoparietal network were compared between a TBI group and a healthy control group [22]. Grossner, Bernier [22] report significant interactions between group and internetwork connectivity of anterior DMN to salience network on explicit self-awareness (R^2=0.13, p=.047). Furthermore, they report significant interactions between group and internetwork connectivity of posterior DMN to salience network on explicit self-awareness (R^2=0.15, p=.038). Specifically, in the TBI group, there were positive relationships between internetwork connectivity and explicit self-awareness, while in the control group these relationships were negative. The anterior DNM included middle and superior frontal regions (shaded area 4a in figure 5); the salience network included the insular cortex and ACC (shaded area 4c in figure 5); the posterior DMN included PCC, precuneus, and temporal poles [shaded area 4b in figure 5; 22].

Summary Performance-Based Discrepancy Method

Five good quality studies investigated neural correlates of impaired self-awareness as measured by performance-based discrepancy scores. Regarding demographics, four studies were rather similar and included populations of moderate to severe TBI patients with a larger proportion of males than females. One study population stood out from the rest with a slightly larger proportion of females, mean age of 61.9 years, and participants had suffered a fronto-insular stroke [21]. This study might be less comparable to the others. Results of Ham, Bonnelle [24] and Grossner, Bernier [22] should be interpreted with caution since they did not correct for multiple testing. Behavioral results concerning implicit self-awareness are mixed, and so are the structural imaging results. Brain areas functionally associated with implicit self-awareness after ABI included the ACC, frontal gyrus, left insula, and parietal operculum. These areas overlap with the networks of which internetwork connectivity is associated with explicit self-awareness. While no behavioral discrepancies between ABI and control groups were found on explicit self-awareness tasks, the imaging results do indicate differences. Again, structural results are mixed. Functional imaging results indicate more BOLD response in ABI patients compared to controls in the ACC, precuneus, and right anterior temporal pole during a self-related task. Furthermore, the association between explicit self-awareness and internetwork connectivity of anterior/posterior DMN to salience network in ABI patients is the opposite of that in healthy controls.

Figure 5. Structural and functional neural correlates of impaired explicit self-awareness as measured with performance-based discrepancy scores after ABI.



Note. **1.** Ventromedial frontal lesions associated with explicit self-awareness [25]. **2**. Lack of positive association, that is present in healthy controls, between explicit self-awareness and gray matter volume in the: **2a.** left posterior region (posterior dorsal and ventral parts of the cingulate cortex, angular gyrus and supramarginal gyrus); **2b.** left orbital region (orbital gyrus and orbital H-shaped sulcus); **2c.** left dorsolateral region (superior & middle frontal gyrus, middle frontal sulcus) in TBI patients [20]. **3**. During self-related task, increased activation in **3a**. right anterior temporal pole, **3b**. anterior cingulate cortex, and **3c.** precuneus in TBI compared to healthy controls [23]. **4**. Explicit self-awareness is positively associated with internetwork connectivity between **4a.** anterior default mode network (blue; middle and superior frontal regions) and **4c**. salience network (purple; insular cortex and anterior cingulate); and between **4b.** posterior default mode network (yellow; posterior cingulate, precuneus and temporal pole) and **4c**. salience network (purple; insular cortex and anterior cingulate) in TBI patients (opposite associations for controls) [26].

Discussion

Self-awareness is crucial for rehabilitation outcome but often impaired after ABI. Understanding the underlying neural correlates of self-awareness of cognitive, emotional, and behavioral deficits after ABI is important for theoretical comprehension as well as the development of measurement instruments and interventions. Therefore, the literature on structural and functional neural correlates of self-awareness was systematically reviewed. Eight studies of poor to good quality were included and results were reported in relation to the different measurement methods and levels of self-awareness. A distinction was made between self-proxy discrepancy scores and performance-based self-awareness scores.

Overall, the current review gives insight into the neural consequences of ABI on self-awareness. Individuals who suffered an ABI show altered functioning and connectivity in brain networks that are associated with self-awareness. The results confirm that the frontal lobes are associated with changed and often impaired self-awareness after ABI, as suggested by Stuss [7]. Moreover, they propose a network approach in which other regions are important too. Namely, a neural network of frontal and cortical midline regions corresponding to the anterior DMN (including middle and superior frontal regions), posterior DMN (including PCC, precuneus and temporal poles), and the salience network (including the insular cortex and ACC).

Theoretical integration

Self-awareness of deficits is theoretically complex and there is a variety of terms to describe the construct. They all refer to a mismatch between an objective and subjective perceived level of functioning. As described in Brown, Fish [8], most models of self-awareness make a distinction between online and offline awareness. Online awareness refers to awareness of one's performance during a task, while offline awareness refers to reflecting on one's behavior before or after a task. Measuring self-awareness using self-proxy discrepancy scores on a questionnaire including multiple domains requires judgments of one's deficits as well as integration of this knowledge into a timeframe. Therefore, this reflects offline awareness. In the model described by Stuss (1991), this would be the highest level of awareness. In the pyramid model by Crosson, Barco [25] this would entail anticipatory awareness, which is comparable to metacognitive knowledge in the model described by Toglia and Kirk [26]. The current review demonstrates that an impairment in this type of self-awareness is associated with lesions and decreased neural functioning in the right frontal lobe, as well as increased diffusivity throughout the white matter of the brain. One performance-based study investigated self-related brain activity, which fits in this highest level of self-awareness too. TBI patients showed over-activation in ACC, precuneus, and right anterior temporal pole during the self-related task compared to healthy controls.

Measuring online self-awareness as a performance-based discrepancy can reflect either the second or the lowest level in the model described by Stuss [7]. The implicit performance-based studies, in which participants had to show adaptive goal-directed behavior during a task, reflect the second level of self-awareness. This corresponds to emergent awareness in the pyramid model [25], and online awareness in Toglia and Kirk's (2000) model. An impairment on this level is associated with less functional connectivity of the ACC and right and middle inferior frontal gyri to the FPCN, as well as more activation in the left insula and left parietal operculum during error processing. The lowest level of self-awareness (knowledge of an impairment or recognition of mistakes made in tasks), reflects intellectual awareness, or a phase in between intellectual and emergent awareness, in the pyramid model [25] and part of metacognitive knowledge in the model described by Toglia and Kirk [26]. This was associated with internetwork connectivity of anterior/posterior DMN to salience network. Specifically, in TBI patients more internetwork connectivity at rest was associated with better self-awareness.

Comparison to healthy individuals and other patient populations

Our findings are in line with previous research in healthy populations in which reflecting on the self, the highest level of self-awareness, was associated with cortical midline structures [10, 11] and the DMN [12]. Anterior components of the DMN are suggested to be involved in perception and judgement, while the posterior components are important for episodic memory retrieval [27, 28]. More specifically, it has been suggested that the PCC regulates self-related processes and is influenced by the mPFC, which can gate this information into conscious awareness by weighing internal and external demands [12]. Furthermore, the connection between DMN and salience network is involved in cognitive control [29]. We found that after ABI, this internetwork connectivity is associated with better self-awareness. The salience network consists of the ACC and insula. The

ACC is associated with performance monitoring. It can detect errors, assess task performance, and signal for behavioral change [29]. The results in this systematic review suggest that after ABI, the ACC is less functionally connected to the FPCN and that this is associated with poor self-awareness in terms of error-correction (second level of awareness). The ACC also showed more BOLD activation during a self-reflection awareness task (highest level of awareness) in the ABI population compared to healthy controls, while behavioral results were similar. These results suggest a role of the ACC in self-awareness (deficits) after ABI.

Individuals diagnosed with Alzheimer's disease (AD) also frequently show impaired self-awareness. The DMN is known to be affected in AD [30]. In line with our results, a recent review concluded that reduced functional connectivity within the DMN in mild to moderate AD is associated with impaired self-awareness measured by questionnaires or self-report [31]. Furthermore, in the initial stages of cognitive decline in AD, impaired self-awareness is associated with neural dysfunction in cortical midline structures, including mPFC, ACC, and PCC. This later progresses to the parietotemporal structures, and, ultimately, to frontotemporal dysfunction [31]. Brain damage after ABI is not neurodegenerative like in AD. Nevertheless, the brain areas found in later stages of AD correspond with these results that show involvement of midline as well as parietotemporal and frontal structures in self-awareness after ABI. However, how these areas influence each other and the generation of awareness remains unclear.

Considerations and future directions

Different measures of self-awareness were used in the studies included in this systematic review. On a behavioral level, the self-proxy discrepancy methods showed significant differences between groups, while performance-based methods often did not. This could be explained by the fact that they measure different levels of awareness. It is important to have these various instruments to be able to measure all aspects of self-awareness. However, it is difficult to compare results within one level of awareness when different instruments are used to measure the same aspect of awareness. The self-proxy discrepancy methods are comparable in that they all compare a patient's own estimation to that of a primary caregiver or relative. However, these questionnaires are somewhat different in what they measure. Some measure estimations of performance, while others measure estimations of impairments. Some focus solely on post-injury status, while others compare pre-injury to post-injury status. Therefore, it is important to consider which questionnaires to use at which time points when studying the variance in self-awareness deficits. Nevertheless, they all measure distinct aspects of the highest level of self-awareness and, as such, all contribute to the understanding of self-awareness.

For the performance-based methods, two types of awareness can be measured: recognition of mistakes and adjustment of one's behavior. In the latter, it is assumed that proper self-awareness is necessary for adaptive goal-directed behavior. However, it is important to realize that some of these implicit awareness tasks might have measured other behaviors such as risk-taking or inhibition. While these factors are linked to self-awareness, these behaviors are not equivalent to self-awareness. In the explicit performance-based methods, which measure recognition of mistakes, participants had to rate how confident they were of their answer by indicating this on a slider or scale. This was not always compared to actual performance and, therefore, it is not always clear whether there was under-confidence, appropriate confidence, or over-confidence. This can be overcome by using a type II area under the receiver operating characteristic curve (AUROC) as was done in Grossner, Bernier [20] and Grossner, Bernier [22]. This is a sophisticated method that combines one's accuracy on the task with one's subjective confidence rating to create a performance-based self-awareness score [32], and should be considered in future research. Another interesting paradigm to consider in future studies is the judgment of learning paradigm in which participants are asked to estimate how well they expect to perform before doing a task [33]. This was not done in the current studies but might be very relevant since it is part of metacognitive strategy training [34] which, in turn, is one of the therapies known to improve rehabilitation outcomes in ABI patients with impaired self-awareness [35].

A first limitation of this review is that the number of studies explicitly investigating neural correlates of self-awareness after ABI is limited. A meta-analysis of the imaging results was not feasible due to the large variety in awareness measurements, imaging techniques, and study designs. The limited number of studies on this topic could be due to the inherent complexity of recognizing self-awareness deficits and quantifying them. Research has primarily focused on the psychological and behavioral aspects of impaired self-awareness. However, the developments in neuroscience tools over the past years, such as neuroimaging, provide opportunities to bridge this gap in literature and gain further understanding of the neural aspects of self-awareness after ABI. Another consideration to keep in mind is the mixed etiology of acquired brain injury. Studies on both TBI and stroke patients were included in this review. The majority of the studies included in this review were on TBI patients. Therefore, the current results are most relevant to that population. Nevertheless, especially given the low number of studies on this topic, reviewing self-awareness in ABI is a good starting point. Further research could look into the differences between etiologies within ABI, as it might be possible that impaired self-awareness evolves differently in different etiologies. Thirdly, it is important to note that some studies applied multiple imaging techniques and/or self-awareness measurement methods on the same, or parts of the same, population. Therefore, some samples come back several times in this systematic review. It is necessary to conduct more studies with different participants so that results are more generalizable. Some of these studies did not correct for multiple testing. Although this was considered in the quality assessment, these results must be interpreted with caution. Lastly, studies on self-awareness of physical or motor deficits were excluded in the current systematic review. While this may limit the generalizability, this approach increases the specificity of our results. Self-awareness of cognitive and behavioral deficits are found to be unrelated to self-awareness of physical deficits [e.g. 15]. Given the complexity of impaired self-awareness and that the level of self-awareness can differ per domain, focusing on the cognitive domain increases the specificity of the results and, hence, the clinical utility.

The current review indicates that brain areas within the salience network and the DMN are involved in self-awareness. Activity and functional connectivity in resting state as well as during tasks are affected after ABI and should be further examined. There is a need for studies using multiple imaging techniques and a combination of self-awareness measurement methods to gain insight into different types of self-awareness within the same population. These studies can provide useful information that can be used to compare self-awareness after ABI to other populations, verify theoretical models, and improve interventions. For example, a recent development in the literature is combining targeted brain stimulation with cognitive rehabilitation. Brain stimulation can enhance brain plasticity and, in combination with cognitive therapy, create a synergistic effect that enhances the effectiveness of rehabilitation [36, 37]. This could be relevant for self-awareness since network functioning appears to be disturbed and, if that can be manipulated, this could aid rehabilitation.

In conclusion, knowledge of impairments, controlling behavior accordingly, and future anticipation of the self in specific situations are distinct aspects of self-awareness that unite in adaptive behavior. Different measurement methods and MRI techniques have been used to assess the neural correlates of self-awareness at each level. Overall, areas of the DMN and salience network were consistently found to be involved in self-awareness after ABI. More research is needed to confirm these findings and further investigate the role of these brain areas in the different levels of self-awareness (deficits) after ABI.

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Appendix 1: Search terms

Pubmed (N=2390)

Anosognosia[Mesh] OR "Diagnostic Self Evaluation"[Mesh] OR Awareness[Mesh] OR Consciousness[Mesh] OR Metacognition[Mesh] OR denial[Mesh] OR self-perception[Mesh] OR self-concept[Mesh] OR Anosognosia*[tiab] OR "Diagnostic Self Evaluation"[tiab] OR awareness[tiab] OR consciousness[tiab] OR metacognition[tiab] OR self-regulat*[tiab] OR unaware*[tiab] OR insight[tiab] OR denial[tiab] OR self-perception[tiab] OR self-concept[tiab] OR self-appraisal[tiab] OR self-conscious*[tiab]

AND

"Brain Injuries"[Mesh] OR Stroke[Mesh] OR "brain injur*"[tiab] OR "brain trauma*"[tiab] OR "acquired brain injury"[tiab] OR stroke[tiab] OR "traumatic brain injury"[tiab] OR "brain lesion*"[tiab] OR "brain damage"[tiab] OR "cerebral injur*"[tiab] OR "cerebral trauma*"[tiab] OR "cerebral lesion*"[tiab] OR "cerebral damage"[tiab] OR "traumatic brain*"[tiab] OR "axonal injur*"[tiab]

AND

Neuroimaging[Mesh] OR "Functional Neuroimaging"[Mesh] OR "Magnetic Resonance Imaging"[Mesh] OR "Diffusion Tensor Imaging"[Mesh] OR "Diffusion Magnetic Resonance Imaging"[Mesh] OR "brain mapping"[Mesh] OR neuroimaging[tiab] OR "functional neuroimaging"[tiab] OR ("magnetic resonance"[tiab] AND (image[tiab] OR images[tiab] OR imaging[tiab])) OR "Diffusion tensor"[tiab] OR diffusion[tiab] OR connectivity[tiab] OR "brain mapping"[tiab] OR activation[tiab] OR voxel[tiab]

Web of Science (N=2972)

TS=(Anosognosia OR "Diagnostic Self Evaluation" OR Awareness OR Consciousness OR Metacognition OR insight OR self-appraisal OR self-conscious* OR Denial OR self-perception OR self-concept OR self-regulat* OR unaware*) OR TI=(Anosognosia OR "Diagnostic Self Evaluation" OR Awareness OR Consciousness OR Metacognition OR insight OR self-appraisal OR self-conscious* OR Denial OR self-perception OR self-concept OR self-regulat* OR unaware*)

AND

TS=("Brain Injuries" OR stroke OR "Brain Disorders" OR "Traumatic Brain Injury" OR "Head Injuries" OR "Traumatic Brain Injury" OR "Trauma" OR "Head Injuries" OR "Brain Damage") OR TI=("Brain Injuries" OR stroke OR "Brain Disorders" OR "Traumatic Brain Injury" OR "Head Injuries" OR "Traumatic Brain Injury" OR "Trauma" OR "Head Injuries" OR "Brain Damage")

AND

TS=("Functional Magnetic Resonance Imaging" OR "Magnetic Resonance Imaging" OR "Neurobiological Measures" OR "Neuroimaging" OR "Brain Connectivity" OR "Diffusion Tensor Imaging" OR diffusion OR connectivity OR activation OR voxel) OR TI=("Functional Magnetic Resonance Imaging" OR "Magnetic Resonance Imaging" OR "Neurobiological Measures" OR "Neuroimaging" OR "Brain Connectivity" OR "Diffusion Tensor Imaging" OR diffusion OR connectivity OR activation OR voxel)

PsycINFO (N=724)

DE Anosognosia OR DE Awareness OR DE Metacognition OR DE self-perception OR DE self-concept OR DE insight OR DE denial DE "Body Awareness" OR DE "Consciousness Disorders" OR TI Anosognosia* OR TI "Diagnostic Self Evaluation" OR TI awareness OR TI consciousness OR TI metacognition OR TI self-regulat* OR TI unaware* OR TI insight OR TI denial OR TI self-perception OR TI self-concept OR TI self-appraisal OR TI self-conscious* OR TI insight OR TI denial OR TI "Consciousness Disorders" OR AB Anosognosia* OR AB "Diagnostic Self Evaluation" OR AB awareness OR AB consciousness OR AB metacognition OR AB self-regulat* OR AB unaware* OR AB insight OR AB denial OR AB self-perception OR AB self-concept OR AB self-appraisal OR AB self-conscious* OR AB insight OR AB denial OR AB "Consciousness Disorders"

AND

DE "Brain Injuries" OR DE "Brain Disorders" OR DE "Traumatic Brain Injury" OR DE "Head Injuries" OR DE "Traumatic Brain Injury" OR DE "Trauma" OR DE "Head Injuries" OR DE "Brain Damage" OR TI "Brain Injuries" OR TI "Brain Disorders" OR TI "Traumatic Brain Injury" OR TI "Head Injuries" OR TI "Traumatic Brain Injury" OR TI "Trauma" OR TI "Head Injuries" OR TI "Brain Damage" OR AB "Brain Injuries" OR

AB “Brain Disorders” OR AB “Traumatic Brain Injury” OR AB “Head Injuries” OR AB “Traumatic Brain Injury” OR AB “Trauma” OR AB “Head Injuries” OR AB “Brain Damage”

AND

DE “Functional Magnetic Resonance Imaging” OR DE “Magnetic Resonance Imaging” OR DE “Neurobiological Measures” OR DE “Neuroimaging” OR DE “Brain Connectivity” OR DE “Diffusion Tensor Imaging” OR TI “Functional Magnetic Resonance Imaging” OR TI “Magnetic Resonance Imaging” OR TI “Neurobiological Measures” OR TI “Neuroimaging” OR TI “Brain Connectivity” OR TI “Diffusion Tensor Imaging” OR AB “Functional Magnetic Resonance Imaging” OR AB “Magnetic Resonance Imaging” OR AB “Neurobiological Measures” OR AB “Neuroimaging” OR AB “Brain Connectivity” OR AB “Diffusion Tensor Imaging”

EMBASE (N=1843)

Anosognosia/ OR Diagnostic Self Evaluation/ OR Awareness/ OR Consciousness/ OR Metacognition/ OR insight/ OR self-appraisal/ OR Anosognosia.tw OR Diagnostic Self Evaluation.tw OR Awareness.tw OR Consciousness.tw OR Metacognition.tw OR insight.tw OR self-appraisal.tw OR self-conscious*.tw

AND

brain injury/ OR brain damage/ OR cerebral damage/ OR traumatic brain injury/ OR brain injury.tw OR brain damage.tw OR cerebral damage.tw OR traumatic brain injury.tw

AND

Functional Magnetic Resonance Imaging/ OR Magnetic Resonance Imaging/ OR Neurobiological Measures/ OR Neuroimaging/ OR Brain Connectivity/ OR Diffusion Tensor Imaging/ OR Functional Magnetic Resonance Imaging.tw OR Magnetic Resonance Imaging.tw OR Neurobiological Measures.tw OR Neuroimaging.tw OR Brain Connectivity.tw OR Diffusion Tensor Imaging.tw OR voxel.tw OR brain mapping.tw

Supplementary material

Table S1. Quality assessment Tezuka et al. (2013)

	+	+/-	-	Other*
1. Did they give a full description of the study participants? (in- and exclusion criteria and patient demographics)		X		
2a. Did they give a full description of the imaging procedure and instructions?		X		
2b. Did they give a full description of the psychological task (measure of awareness) used?	X			
3. Did they specify the spatial normalization procedure, including the atlas or template which is used to match the images to?			X	NR
4. Did they specify how the regions of interest were determined?		X		
5. Did they provide enough detail to reproduce the analysis?		X		
6. Are all the empirical claims supported by a specific statistical test?		X		
7. Did they describe and account for the multiple testing problem?				NA
8. Do the figures and tables stand on their own?	X			
9. Are the quality control measures documented?			X	NR
Quality Rating (Good, Fair or Poor): Fair	**4.5 out of 9 → 5**			

Additional Comments (If poor, please state why): 2a) Describe that they did T1/T2 weighted images, not how. 3) Not reported. 4) Not regions of interest but hemispheres. Only describe that neurologists evaluated cerebrovascular disease, but now how. 6) Not all statistics mentioned.
**NA, not applicable: NR, not reported.*

Table S2. Quality assessment Bivona et al. (2014)

	+	+/-	-	Other*
1. Did they give a full description of the study participants? (in- and exclusion criteria and patient demographics)	X			
2a. Did they give a full description of the imaging procedure and instructions?			X	
2b. Did they give a full description of the psychological task (measure of awareness) used?	X			
3. Did they specify the spatial normalization procedure, including the atlas or template which is used to match the images to?			X	
4. Did they specify how the regions of interest were determined?			X	
5. Did they provide enough detail to reproduce the analysis?			X	
6. Are all the empirical claims supported by a specific statistical test?	X			
7. Did they describe and account for the multiple testing problem?			X	NR
8. Do the figures and tables stand on their own?	X			
9. Are the quality control measures documented?			X	NR
Quality Rating (Good, Fair or Poor): Poor	**4 out of 10 → 4**			

Additional Comments (If poor, please state why): 2a) Only mention a scan was made but not how or when. Also not mentioned how they were assessed. 3) No description of who did the neuroimaging examination or how it was done. 4) Only report regions in table 3, not how they were determined. 5) Only described very briefly. 7) Compared groups for multiple brain regions but did not correct for multiple testing.
**NA, not applicable: NR, not reported*

Table S3. Quality assessment Lesimple et al. (2019)

	+	+/-	-	Other*
1. Did they give a full description of the study participants? (in- and exclusion criteria and patient demographics)	X			
2a. Did they give a full description of the imaging procedure and instructions?	X			
2b. Did they give a full description of the psychological task (measure of awareness) used?	X			
3. Did they specify the spatial normalization procedure, including the atlas or template which is used to match the images to?	X			
4. Did they specify how the regions of interest were determined?	X			
5. Did they provide enough detail to reproduce the analysis?	X			
6. Are all the empirical claims supported by a specific statistical test?		X		
7. Did they describe and account for the multiple testing problem?			X	NR
8. Do the figures and tables stand on their own?		X		
9. Are the quality control measures documented?	X			
Quality Rating (Good, Fair or Poor): Good	**8 out of 10 → 8**			

Additional Comments (If poor, please state why): 6) Statistical tests done but not all statistics described. 7) Five measures of white matter integrity were correlated with awareness but no multiple testing correction reported. 8) Abbreviations not explained.
**NA, not applicable: NR, not reported*

Table S4. Quality assessment Schmitz et al. (2006)

	+	+/-	-	Other*
1. Did they give a full description of the study participants? (in- and exclusion criteria and patient demographics)	X			
2a. Did they give a full description of the imaging procedure and instructions?	X			
2b. Did they give a full description of the psychological task (measure of awareness) used?	X			
3. Did they specify the spatial normalization procedure, including the atlas or template which is used to match the images to?	X			
4. Did they specify how the regions of interest were determined?				NA
5. Did they provide enough detail to reproduce the analysis?	X			
6. Are all the empirical claims supported by a specific statistical test?	X			
7. Did they describe and account for the multiple testing problem?	X			
8. Do the figures and tables stand on their own?		X		
9. Are the quality control measures documented?	X			
Quality Rating (Good, Fair or Poor): Good	**8.5 out of 9 → 9.4**			

Additional Comments (If poor, please state why): 3+8) Table 3 mentions MNI space and talaraich coordinates, methods reports MNI. 4) Whole brain analysis.
**NA, not applicable: NR, not reported*

Table S5. Quality assessment Ham et al. (2014)

	+	+/-	-	Other*
1. Did they give a full description of the study participants? (in- and exclusion criteria and patient demographics)	X			
2a. Did they give a full description of the imaging procedure and instructions?	X			
2b. Did they give a full description of the psychological task (measure of awareness) used?	X			
3. Did they specify the spatial normalization procedure, including the atlas or template which is used to match the images to?	X			
4. Did they specify how the regions of interest were determined?	X			
5. Did they provide enough detail to reproduce the analysis?	X			
6. Are all the empirical claims supported by a specific statistical test?		X		
7. Did they describe and account for the multiple testing problem?		X		
8. Do the figures and tables stand on their own?	X			
9. Are the quality control measures documented?	X			
Quality Rating (Good, Fair or Poor): Good	**9 out of 10 → 9**			

Additional Comments (If poor, please state why): 6) Not all behavioral scores have statistics. 7) Correct for multiple testing in MRI analysis. However, investigate different brain regions in ROI analysis and do not report correction for multiple testing there.
**NA, not applicable: NR, not reported*

Table S6. Quality assessment Grossner et al. (2018)

	+	+/-	-	Other*
1. Did they give a full description of the study participants? (in- and exclusion criteria and patient demographics)	X			
2a. Did they give a full description of the imaging procedure and instructions?	X			
2b. Did they give a full description of the psychological task (measure of awareness) used?	X			
3. Did they specify the spatial normalization procedure, including the atlas or template which is used to match the images to?	X			
4. Did they specify how the regions of interest were determined?	X			
5. Did they provide enough detail to reproduce the analysis?		X		
6. Are all the empirical claims supported by a specific statistical test?		X		
7. Did they describe and account for the multiple testing problem?			X	N.R.
8. Do the figures and tables stand on their own?		X		
9. Are the quality control measures documented?	X			
Quality Rating (Good, Fair or Poor): Good	**7.5 out of 10 → 7.5**			

Additional Comments (If poor, please state why): 7) Separately correlated orbital region, dorsolateral region, posterior region, and frontopolar regions to behavioral measure but do not correct for multiple testing. 8) Table 1 no footnotes describing what is between brackets or what abbreviations stand for.
**NA, not applicable: NR, not reported*

Table S7. Quality assessment Grossner et al. (2019)

	+	+/-	-	Other*
1. Did they give a full description of the study participants? (in- and exclusion criteria and patient demographics)	X			
2a. Did they give a full description of the imaging procedure and instructions?	X			
2b. Did they give a full description of the psychological task (measure of awareness) used?	X			
3. Did they specify the spatial normalization procedure, including the atlas or template which is used to match the images to?	X			
4. Did they specify how the regions of interest were determined?	X			
5. Did they provide enough detail to reproduce the analysis?	X			
6. Are all the empirical claims supported by a specific statistical test?	X			
7. Did they describe and account for the multiple testing problem?		X		
8. Do the figures and tables stand on their own?	X			
9. Are the quality control measures documented?	X			
Quality Rating (Good, Fair or Poor): Good	**9.5 out of 10 → 9.5**			

Additional Comments (If poor, please state why): 7) Investigate inter- and intranetwork connectivity for 6 different subsystems but do not correct for multiple testing.
**NA, not applicable: NR, not reported*

Table S8. Quality assessment Garcia-Cordero et al. (2019)

	+	+/-	-	Other*
1. Did they give a full description of the study participants? (in- and exclusion criteria and patient demographics)	X			
2a. Did they give a full description of the imaging procedure and instructions?	X			
2b. Did they give a full description of the psychological task (measure of awareness) used?	X			
3. Did they specify the spatial normalization procedure, including the atlas or template which is used to match the images to?	X			
4. Did they specify how the regions of interest were determined?				NA
5. Did they provide enough detail to reproduce the analysis?		X		
6. Are all the empirical claims supported by a specific statistical test?	X			
7. Did they describe and account for the multiple testing problem?	X			
8. Do the figures and tables stand on their own?	X			
9. Are the quality control measures documented?	X			
Quality Rating (Good, Fair or Poor): Good	**8.5 out of 9 → 9.4**			

Additional Comments (If poor, please state why): 4) Whole brain. 5) Smoothing not reported
**NA, not applicable: NR, not reported*

CHAPTER 5

Impaired self-awareness and denial of disability in a community sample of people with traumatic brain injury

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Abstract

Purpose: To examine the nature and severity of impaired self-awareness (ISA) and denial of disability (DD) in a community-dwelling TBI population. Additionally, to investigate reliability, internal consistency, and feasibility of the Clinician's Rating Scale for evaluating Impaired Self-Awareness and Denial of Disability after brain injury (CRS-ISA-DD).

Materials and methods: ISA and DD were studied using the CRS-ISA-DD in a cross-sectional study with 78 TBI patients (3.1 years post-injury).

Results: Forty-two percent (42%) of individuals approached consented to participate in this study. Most participants showed one or more symptoms of ISA and DD, but severity scores were in the lower range (ISA: 13.2±16.2; DD: 9.4±10.7). The CRS-ISA-DD takes <10 minutes to complete, has excellent inter-rater reliability (ISA: ICC(2,1)=.928; DD: ICC(2,1)=.835), and acceptable-good internal consistency (ISA: α=.819; DD: α=.645). ISA severity correlated with neuropsychological test scores (r_s=-.30 to -.47) and injury severity. DD severity correlated with anxiety (r_s=-.22) but not with avoidance coping or defense mechanisms.

Conclusions: Low levels of ISA and DD occurred in this sample of TBI patients. The CRS-ISA-DD is a reliable and feasible instrument. We recommend using it as diagnostic tool to differentiate between ISA and DD once self-awareness problems have been identified.

Introduction

Traumatic brain injury (TBI) can have neuropsychological consequences for which many people receive rehabilitation treatment. Unfortunately, a proportion of TBI patients suffer from problems of impaired self-awareness. Unawareness of deficits refers to the inability to appraise one's own strengths and weaknesses as well as understand the implications these have for daily life activities [1, 2]. These consequences can persist into the chronic stage, long after patients have been discharged home [3]. Patients who are unaware of their deficits are prone to less independence in complex everyday tasks, worse psychological and/or emotional adjustment, and less favorable employment outcomes compared to patients with good awareness of their deficits [4, 5]. Moreover, TBI patients' self-awareness problems can affect their significant others. For example, self-awareness deficits in the chronic stage correlate with relatives' subjective burden [6]. Therefore, it is important for both the patients as well as their significant others that self-awareness problems are addressed. However, to determine what type of care is most suitable, it is important to know what type of self-awareness deficits they have.

The nature of unawareness of deficits is not completely understood but it is recognized that biological, psychological, and socio-environmental factors are involved [7]. Biological aspects include neurocognitive factors originating from brain dysfunction. Neurocognitive impaired self-awareness of deficits (ISA) is thought to be a direct result of a neurologically based deficiency [8]. This type of unawareness of deficits has been associated with impaired executive functions [9] and injury severity [10-12]. The psychological factor associated with unawareness of deficits, denial of disability (DD), is thought to be the result of psychological avoidance or defensive coping mechanisms [13]. Denial as a coping mechanism protects patients from emotional distress, particularly anxiety [8, 14]. At the socio-environmental level, factors include interactions with friends, family, and colleagues, such as opportunities to experience and recognize changes in functioning [7].

In the past, efforts have been made to distinguish neurocognitive and psychological factors that influence impairments in awareness of deficits. This is especially relevant for clinical practice, but also important in a community context. At first glance, patients with ISA and DD can present alike, reporting no or few problems, but the different types of unawareness might require different treatment approaches. For example, several case studies suggest that patients with ISA require a different therapeutic approach compared to patients with DD. Katz, Fleming, and colleagues [15] describe three case studies with various and complex presentations of unawareness. They report that a patient with unawareness due to neurocognitive disturbance profits from challenging tasks in which they can discover abilities and weaknesses with the help of therapist feedback, while these challenging tasks could risk breaking down defense mechanisms in patients with high levels of DD [15]. The patients with high levels of DD probably benefit most from a more psychotherapeutic approach that involves developing a therapeutic alliance, providing opportunities to seek support, and taking into account the patient's readiness and cognitive impairment [16].

Most instruments used to assess awareness, like the Patient Competency Rating Scale (PCRS), can indicate a general impairment in awareness of deficits but do not differentiate between ISA and DD. To our knowledge, the Clinician's Rating Scale for evaluating Impaired Self-Awareness and Denial of Disability after brain injury (CRS-ISA-DD) developed by Prigatano and Klonoff [8] is the only instrument specifically designed to differentiate between ISA and DD. It consists of two subscales, each enlisting ten behaviors indicative of either ISA or DD. Prigatano and Klonoff [8] investigated the inter-rater reliability and construct validity of the CRS-ISA-DD in a clinical TBI population. In general, inter-rater reliability was high (r=.77). The initial test of construct validity was encouraging, since results showed that patients clinically judged as primarily ISA patients scored significantly higher on the ISA scale than DD patients and vice versa [8]. So far, the scale has only been used in a few studies with clinical populations [8, 15, 17]. Since problems related to impaired self-awareness can persist after discharge home, it is important to investigate the usefulness of this instrument in TBI patients who are reintegrating into the community.

The aim of this study was twofold: (1) to investigate the nature and severity of ISA and DD symptoms in a community-dwelling TBI sample and (2) to investigate psychometric properties of the CRS-ISA-DD. It was hypothesized that the ISA and DD scales would both show a positive association with a frequently used measure of general awareness of deficits, namely, the Patient Competency Rating Scale. In addition, we hypothesized that high ISA scores would be associated with poorer neuropsychological functioning but not, or to a lesser extent, to psychological factors such as anxiety. In contrast, we expected that the DD scale would be associated with measures of avoidance coping, use of defense mechanisms, and anxiety while not, or to a lesser extent, with poorer neuropsychological functioning.

Methods

Participants

Participants were former patients of three rehabilitation centers in the Netherlands and their significant others. The patients had all received in- and/or outpatient rehabilitation but were no longer in active treatment at the moment of recruitment. Recruitment took place from July to November 2013 at Adelante, Libra, and Zuyderland Medical Center, and from March 2017 to June 2018 at Libra and Adelante. This second cohort was added in an attempt to gather data with more variability for the construct validity analysis. Inclusion criteria were minimum age of 18; moderate to severe traumatic brain injury as measured by Post Traumatic Amnesia (PTA) >1 hour or a Glasgow Coma Scale (GCS) score 3-12 or Loss of Consciousness (LOC) >1 hour [18]; between 6 months and 6 years post injury; discharged home after rehabilitation. Exclusion criteria were a premorbid psychiatric disorder that required treatment; language and communication problems; absence of a significant other willing to participate; presence of a statement of refusal to participate in scientific research in the medical file.

A significant other was defined as a person who is close to the patient and knows the patient well, such as a partner or family member. Significant others were eligible for participation if they were 18 years or older and were excluded if they had language and communication problems based on clinical judgment.

Measures

Demographic and injury related information. Socio-demographic data and injury characteristics were collected from medical files. These included age, sex, level of education, date of injury, cause of injury, and initial severity of injury. Level of education was dichotomized into high education, including senior secondary education, university preparatory education, higher professional education and university, and low education, which was primary education or less. Injury severity was reported using the GCS [19], duration of PTA or duration of LOC [18], depending on which clinical data were available.

Impaired self-awareness and denial of disability. The Clinician's Rating Scale for Evaluating Impaired Self-Awareness and Denial of Disability (CRS-ISA-DD) consists of two subscales: Impaired Self-Awareness (ISA) and Denial of Disability (DD). Each subscale consists of ten items on typical behaviors of ISA or DD. For this study, all original items were translated and revised to clarify their meaning (Appendix 2). The assessor rates the presence and severity of the behaviors based on contact with the patient and significant other; in this study this was based on the interview with the patient and significant other and the patient's verbal and nonverbal reactions during neuropsychological testing and feedback. If a behavior is rated as present, severity of the behavior is scored. Severity scores can range from 1 (very mild) to 10 (severe). If a characteristic is not present, the severity score is 0. The total severity score of each subscale was used in the analyses and can range from 0 to 100 with a higher score representing more severe ISA or DD [8].

Feasibility. To assess the feasibility of the CRS-ISA-DD, patients and significant others were asked how uncomfortable and how confronting the assessment procedure was. These items were rated on a scale ranging from 1, very uncomfortable or confronting, to 5, not at all uncomfortable or confronting. In addition, the researchers recorded the time needed to complete the CRS-ISA-DD and they rated the ease to complete the scale. Scores ranged from 1 (very easy) to 5 (very hard).

Awareness of deficits. The Patient Competency Rating Scale (PCRS) is a 30-item self-report instrument [20]. The items measure the patient's degree of difficulty on a variety of tasks and functions on a scale from 1 (can't do) to 5 (can do with ease); total score range is 30 to 150. Both the patient and significant other completed the PCRS. The measure of awareness of deficits is the discrepancy score (patient's total score – significant other's total score) and can range from -120 to 120. The greater the discrepancy, the more impaired the patient's self-awareness of deficits. A negative discrepancy score indicates underestimation of competencies by the patient, while a positive discrepancy score indicates overestimation of competencies.

Neuropsychological assessment. The neuropsychological tasks used were chosen to reflect diverse cognitive functions and give an indication of impairments in these cognitive functions (and underlying brain networks). The Letter Digit Substitution Test (LDST) [21] was used to assess information processing speed. Patients were instructed to match digits with letters according to a key, as many as possible within 90 seconds. There was a written and a verbal version. The number of digits correctly reported after 60 seconds was used as outcome measure. The Visual Verbal Learning Test (VVLT) [22] was administered as a measure of memory performance. Patients were shown a list of 15 words repeated over five trials and were asked to repeat them after each trial (immediate recall) and after 20 minutes (delayed recall). The total number of correct responses over five trials and the number of correct responses on the delayed recall were used as outcome measures. The Halstead Finger Tapping Test (HFTT) [23] measures finger tapping speed and is thought to provide information about brain dysfunction [23-25]. The index finger is placed on a lever and all other fingers rest on the board. Patients were given seven 10-second trails for both the dominant and non-dominant hand. After three trials patients switched hands to avoid fatigue [26]. The outcome measure was the average of seven trials per hand. Phonemic fluency was used as a measure of executive functioning [27, 28]. There were three rounds in which patients had 60 seconds to name as many words as possible starting with either the letter D, A or T. The number of correct items generated was used as outcome measure. The Zoo map test, a measure of planning and executive functioning, is part of the Behavioural Assessment of the Dysexecutive Syndrome [29]. It involves plotting a route through a map following a set of rules. Scores range from 0-16 with higher scores indicating better performance. The Block Design test, part of the Wechsler Adult Intelligence Scale-IV (WAIS-IV) [30], was administered but scores were not calculated. Instead, participants' reactions to the difficult situations and confrontation were noted and used to score the CRS-ISA-DD.

Defense mechanisms. The Defense Mechanism Manual (DMM) was employed to assess the use of defense mechanisms in Thematic Apperception Test (TAT) stories (Cards 2, 3BM, 4, 12F) [31]. The stories were audio recorded, transcribed, translated into English in order to be independently scored by two trained coders (JP and RK) on the presence of three defense mechanisms: denial, projection, and identification. Scores were summed to obtain a DMM total score with higher scores indicating more use of overall defense mechanisms. Relative scores per defense were calculated by dividing the scores of each defense by the sum of all three defense scores. The method has good inter-rater reliability scores (r=.82 for Denial, r=.71 for Projection, r=.82 Identification) [31].

Avoidance coping. The COPE Inventory [32] is a 60-item self-report questionnaire measuring coping responses with scores from 1 (I usually don't do this a all) to 4 (I usually do this a lot). Items are organized into 15 separate scales. In this study, three subscales were used: denial, mental disengagement, and behavioral disengagement. Together these subscales form the second-order factor avoidance coping which has a score range of 12 to 48 and higher scores represent more use of avoidance coping [17].

Anxiety. The anxiety subscale of the Hospital Anxiety and Depression Scale (HADS-A) was used to determine patients' levels of anxiety [33]. The HADS-A contains seven items scored on a 4-point scale ranging from 0 to 3. Higher scores reflect a higher amount of reported anxiety symptoms.

Study procedures

The patients' former treating physician or psychologist screened the patient files for eligibility. They informed patients and significant others and asked for interest in participation. A researcher then contacted the patient, gave more information if necessary and, if both patient and significant other agreed, planned a visit. After obtaining written informed consent, a researcher carried out the assessment procedure at the patient's home.

The assessment procedure was held in Dutch. First, a standardized neuropsychological interview with the patient and significant other was held that lasted approximately 30 minutes (Appendix 1). They were asked to share their views on changes due to the TBI with a focus on the patient's cognitive impairment, emotional changes, and problems in daily functioning. This was videotaped to allow two researchers to independently analyze it. Next, patients completed the neuropsychological tests and questionnaires. Significant others completed a questionnaire about the patient's functioning. Oral feedback about performance on the neuropsychological tests was given immediately and patients' verbal and nonverbal reactions during neuropsychological testing and feedback were noted. Finally, patients and significant others completed a short feasibility questionnaire. Both researchers noted the CRS-ISA-DD administration time and completed a questionnaire on its feasibility.

Ethical approval for this study was obtained from the ethics committee of the Maastricht University Medical Center (MUMC) with reference number NL42752.068.12. The study was conducted according to the principles of the Declaration of Helsinki (World Medical Association, October 2008) and in accordance with the Medical Research Involving Human Subjects Act (WMO).

Statistical analyses

All statistical analyses were conducted using SPSS 25 for Windows. Results were considered significant if $p \leq .05$.

Demographic and injury related information. Descriptive statistics were used to describe the demographic and injury related parameters. The following neuropsychological test scores were transformed to standardized Z- and T-scores derived from norm data: LDST [21], VVLT [34], HFFT [35] and phonemic fluency [36]. In line with the scoring instructions, data of the COPE were discarded if more than one item on a subscale was missing. PCRS and HADS-A data was discarded if more than 25% of the items were missing. If for any scale the amount of missing items was within the allowed range, the total score was calculated by extrapolating the total score of the items available ((total score/#completed items)*total #items on scale).

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Nature and severity ISA and DD. Descriptive statistics were used to describe the presence of one or more symptoms of ISA and DD, as well the severity of these symptoms.

Inter-rater reliability. Two raters, both neuropsychologists, completed the CRS-ISA-DD independently of each other in order to determine inter-rater reliability using intra-class correlations (ICC). The appropriate type of ICC, i.e., ICC(2,1), was determined based on the description by Shrout and Fleiss [37]. The estimate for absolute agreement between raters was reported. An ICC>.74 is considered excellent, .74 to .60 is considered good, .59 to .40 is considered fair and <.40 is considered poor [38]. This was completed on the first cohort only. The rater for the second cohort was also a rater in the first cohort.

Internal consistency. Internal reliability of the ISA and DD scales was assessed using Cronbach's alpha. A Cronbach's alpha ≥.8 was considered good, .70-.80 moderate, .60-.70 acceptable and <.60 was considered as poor internal consistency [39].

Floor and ceiling effects. Floor or ceiling effects were considered present if more than 15% of the patients had the highest or lowest possible score on either the ISA or DD scale [40].

Feasibility. To explore the feasibility, the mean time of the CRS-ISA-DD assessment and frequency counts of the different answers on the feasibility questionnaire were calculated.

Correlations with other measures. Because of violations of the normality assumption, Spearman's correlation coefficients were used to investigate associations between the CRS-ISA-DD subscales and injury severity, PCRS discrepancy score, neuropsychological test scores, COPE Avoidance, DMM, and HADS-A. Correlations were considered good if ≥.60, moderate between .30 and .60, and poor for correlations ≤.30 [39].

Results

Participants

Seventy-eight patients and significant others consented to participate, corresponding to a 42% response rate. Although not explicitly asked, some patients and significant others who refused to participate gave reasons for refusal. They found it too time-consuming, too confronting, did not see a need to participate or thought the injury was too long ago and wanted to close that chapter of their life. In some cases, there were no significant others available or willing to participate. Some significant others anticipated a quarrel with the patient since they disagreed about the experienced difficulties and, therefore, chose not to participate.

Patient characteristics are presented in table 1. The majority of the significant others were partners (n=43; 55%) or parents (n=23; 30%). Of the remaining significant others, five were the patient's children, three were siblings, two were neighbors and one was an ex-partner. With respect to missing values, the following amount of data was discarded because the amount of missing items was out of range: two PCRS patient questionnaires, two HADS-A questionnaires, and three COPE avoidance scales. Feasibility data was missing and discarded for three patients and seven significant others. There were no missing values in the CRS-ISA-DD data.

Nature and severity ISA and DD

Regarding the scores on the CRS-ISA-DD, at least one item was scored as present for most participants on the ISA scale (N=57) as well as the DD scale (N=58). Eleven participants showed presence of more than three items on ISA, and seven participants showed presence of more than three items on DD. If present, severity was scored. As can be seen in figure 1, the severity scores on the ISA and DD scales were skewed to the left. The majority of the patients had a severity score in the lower range on both scales, indicating that most patients had little awareness deficits and only a few patients showed severe ISA and/or DD. The correlation between the ISA and DD scales was not significant ($r_s(76)=-.07$, p=.54).

Inter-rater reliability

For the first cohort of participants included in the study, a second rater independently rated the CRS-ISA-DD data (N=57). Inter-rater reliability was excellent on both scales. The ICC(2,1) absolute agreement coefficient was .928 (p<.00, 95% CI = .881-.957) for the ISA scale and .835 (p<.00, 95% CI = .735-.899) for the DD scale.

Table 1. Sample characteristics (N=78)

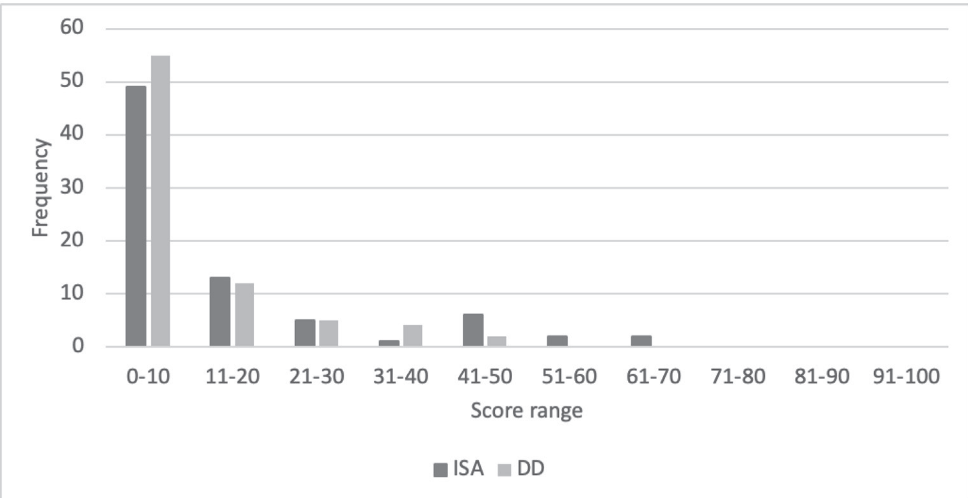
		Frequency (%)	
Female		21 (26.9)	
Male		57 (73.1)	
Level of education	Low	35 (44.9)	
	High	43 (55.1)	
Cause of TBI	Motor vehicle accident	39 (50.0)	
	Fall	34 (43.6)	
	Violence	3 (3.7)	
	Industrial accident	1 (1.3)	
	Unknown	1 (1.3)	
		Mean (±SD)	**Range**
Age		46.6 (17.8)	19-79
Years post injury		3.1 (1.5)	.6-6.0
Severity of TBI	GCS (n=53)	6.5 (3.5)	3-15
	PTA (days) (n=39)	19.8 (27.9)	.02-106.5
	LOC (days) (n=31)	14.6 (22.1)	0-120
ISA sum score		2.2 (2.2)	0-8
ISA severity score		13.2 (16.2)	0-67
DD sum score		1.67 (1.7)	0-6
DD severity score		9.4 (10.7)	0-43
PCRS discrepancy score		3.0 (12.5)	-25.4-28.2
PCRS total score patient		114.7 (17.2)	80-150
PCRS total score relative		111.7 (18.9)	60-148
LDST 60sec writing (z-score)		-.94 (1.2)	-3.9-3.0
LDST 60sec verbal (z-score)		-1.3 (1.0)	-5.0-.7
VVLT total score (z-score)		.05 (1.3)	-3.0-2.8
VVLT delayed recall (z-score)		-.26 (1.2)	-2.8-1.7

Table 1. Continued

	Mean (±SD)	Range
HFTT left hand (t-score)	39.1 (12.0)	0-64
HFTT right hand (t-score)	40.4 (11.8)	6-73
Fluency (t-score)	45.6 (11.7)	22-84
Zoo map test	10.3 (5.0)	-8-16
COPE inventory avoidance	21.7 (5.1)	12-35
DMM total	10.3 (5.8)	1-38
Denial total score	3.5 (2.1)	0-13
Projection total score	3.6 (3.8)	0-22
Identification total score	3.2 (2.4)	0-13
HADS-Anxiety	6.0 (3.6)	0-14

Note. High education included senior secondary education, university preparatory education, higher professional education and university. Low education included primary education or less. TBI=traumatic brain injury; MVA=motor vehicle accident ; GCS=Glasgow Coma Scale ; PTA=Post-Traumatic Amnesia; LOC=loss of consciousness; ISA=Impaired self-awareness; DD=Denial of Disability; PCRS=Patient Competency Rating Scale; DMM=Defense Mechanism Manual; LDST=Letter Digit Substitution Test; VVLT=Visual Verbal Learning Test; HFTT=Halstead Finger Tapping Test; HADS=Hospital Anxiety and Depression Scale

Figure 1. Distribution of the severity scores on the Impaired Self-Awareness (ISA) scale and the Denial of Disability (DD) scale.



Internal consistency

The internal consistency of the ISA scale was good (Cronbach's alpha = .819). The DD scale had an acceptable internal consistency (Cronbach's alpha =.645).

Floor and ceiling effects

Indications of floor effects were found on both scales. On the ISA scale, 19 patients (24.4%) scored the lowest possible score. On the DD scale, 20 patients (25.6%) scored the lowest possible score. None of the participants obtained the highest possible score on the ISA or DD scale, indicating no ceiling effects.

Feasibility

The majority of the participants who filled out the feasibility questionnaires did not experience the assessment procedure as uncomfortable (patients: 84%, N=63; significant others: 93%, N=66; score >3) or confronting (patients: 73%, N=55; significant others 79% N=56; score >3).

For the subset of 57 participants assessed by two raters, assessment time was noted. The neuropsychological interview and assessment took approximately 2.5 hours in total. To complete the CRS-ISA-DD, the raters on average needed 8.3 minutes (SD=3.2, range 5-17.5). Once familiar with the scale, the rating duration decreased. Seventy-seven percent of the ratings were made within 5 to 10 minutes. The two raters indicated that for the majority of the ratings (65%) the CRS-ISA-DD was easy to very easy (score < 3) to score.

Correlations with other measures

The results of the analysis of the associations between the ISA and DD scale and the injury severity measures, PCRS discrepancy scores, neuropsychological assessment, COPE Avoidance, DMM and HADS-A scores can be found in table 2.

Injury severity measures. It was uncommon for all three measures of injury severity to be noted in the medical files. In eight cases, the GCS, PTA as well as LoC scores were available. In 32 cases, only two of these were available, in 35 cases, only one was available, and in three cases, none was available. Classifying patients into groups based on different measurements can lead to inconsistencies. Therefore, each injury severity measure was used as a continuous variable and separately correlated with ISA and DD. The ISA scale showed moderate significant associations with GCS score (r_s(51)=-.32, p=.02), longer duration of PTA (r_s(37)=.37, p=.02) as well as LOC (r_s(29)=.42, p=.02). These results indicate that the more severely injured someone was, the higher their ISA scores. The DD scale, on the other hand, was not significantly associated with GCS (r_s(51)=-.04, p=.77), duration of PTA (r_s(37)=.08, p=.63) or duration of LOC (r_s(29)=-.13, p=.47).

Table 2. Relationships between the ISA and DD scale and other measures

	ISA severity	**DD severity**
GCS	-.32*	-.04
PTA	.37*	.08
LOC	.42*	-.13
PCRS discrepancy score	-.03	-.01
Neuropsychological assessment		
LDST 60 sec writing (z-score)	-.30**	.01
LDST 60 sec verbal (z-score)	-.22	.07
VVLT total score (z-sore)	-.47**	.05
VVLT delayed recall (z-score)	-.45**	.07
HFFT left hand (T-score)	-.17	.07
HFFT right hand (T-score)	-.08	.03
Fluency (T-score)	-.21	.04
Zoo map test raw score	-.39**	.17
COPE Inventory Avoidance	.11	-.14
Total defense mechanism score TAT	-.15	.05
Denial relative score	.24*	-.18
Projection relative score	-.24*	.04
Identification relative score	-.04	.20
HADS anxiety	-.05	-.22*

*p ≤.05, ** p ≤.001

Note. ISA=Impaired Self-Awareness; DD=Denial of Disability; GCS=Glasgow Coma Scale; PTA=Post-Traumatic Amnesia; LOC=Loss of Consciousness; PCRS=Patient Competency Rating Scale; LDST=Letter Digit Substitution Test; VVLT=Visual Verbal Learning Test; HFTT=Halstead Finger Tapping Test; DMM=Defense Mechanism Manual; HADS=Hospital Anxiety and Depression Scale.

Awareness of deficits. No associations were found between the PCRS discrepancy scores and either ISA (r_s(74)=-.03, p=.78) or DD scales (r_s(74)=-.01, p=.92). In general, PCRS discrepancy scores were low (M=3.0, SD=12.5) indicating that, on average, patients had good awareness of their deficits.

Neuropsychological assessment. With respect to the neuropsychological measures, significant negative associations were found between the ISA scale and the written version of the LDST ($r_s(74)=-.30$, $p=.01$), the VVLT total score ($r_s(76)=-.47$, $p<.001$), VVLT delayed recall score ($r_s(76)=-.45$, $p<.001$) and the Zoo map test ($r_s(75)=-.39$, $p<.001$). These moderate associations indicate that worse cognitive performance is associated with more severe ISA. No significant associations were found between the ISA scale and the verbal version of the LDST ($r_s(74)=-.22$, $p=.06$), phonemic fluency ($r_s(76)=-.21$, $p=.06$) or the HFFT (left $r_s(75)=-.17$, $p=.14$; right $r_s(76)=-.08$, $p=.51$). None of the neuropsychological measures correlated significantly with the DD scale: written version of the LDST ($r_s(74)=.01$, $p=.94$), verbal version of the LDST ($r_s(74)=.07$, $p=.58$), the VVLT total score ($r_s(76)=.05$, $p=.68$), VVLT delayed recall score ($r_s(76)=.07$, $p=.55$), HFFT (left $r_s(75)=.07$, $p=.52$; right $r_s(76)=.03$, $p=.77$), phonemic fluency ($r_s(76)=.04$, $p=.70$), Zoo map test ($r_s(75)=.17$, $p=.15$).

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Avoidance coping. No significant associations were found between the COPE Inventory Avoidance factor and either ISA ($r_s(73)=.11$, $p=.37$) or DD scales ($r_s(73)=-.14$, $p=.22$).

Defense mechanisms. Total defense mechanism scores were not significantly correlated with either ISA ($r_s(74)=-.15$, $p=.19$) or DD scale ($r_s(74)=.05$, $p=.67$). On the DMM subscales, ISA showed low but significant associations with the use of denial ($r_s(74)=.24$, $p=.04$) and projection ($r_s(74)=-.24$, $p=.03$), and no significant associations with identification ($r_s(74)=-.04$, $p=.71$). Thus, more severe ISA was associated with more use of denial and less use of projection as a defense mechanism. None of the DMM subscales correlated significantly with the DD scale (denial ($r_s(74)=-.18$, $p=.11$); projection ($r_s(74)=.04$, $p=.74$); identification ($r_s(74)=.20$, $p=.09$)).

Anxiety. HADS-A scores were not significantly associated with ISA scores ($r_s(74)=-.05$, $p=.67$). However, the correlation between anxiety scores and DD scores was significant ($r_s(74)=-.22$, $p=.05$) and indicates that patients with more severe DD report fewer anxiety symptoms.

Discussion

The aim of this study was to investigate the nature and severity of ISA and DD symptoms in a community-dwelling TBI sample and to assess the psychometrics properties of the CRS-ISA-DD. The current sample showed symptoms of impaired self-awareness. The majority of the participants showed presence of at least one ISA or DD behavior, indicating ISA and DD occur in community-dwelling TBI patients. Sometimes the ISA or DD was fairly severe. Nonetheless, there were not many participants with extreme severity scores, especially regarding DD.

The variability in scores on the ISA and DD scales was low. Our sample consisted of mostly patients with good awareness and only a few who showed higher levels of ISA and/or DD. The floor effect for the ISA and DD scales also indicates a reduced variability in the gathered data. The lack of patients with more severe awareness deficits in our sample may have influenced the statistical power. Denial could serve as a mechanism to protect oneself against the immediate impact of a life-changing event, such as TBI, and could act as a buffer during which more adaptive coping strategies can be developed [41]. Even though some patients with DD were present in the current sample, it is possible that the more extreme cases were missed or that DD is more frequently present in the acute post-injury phase. In case of the latter, the CRS-ISA-DD might be less suitable for use as a screening tool in chronic community-dwelling patients and more suitable earlier in the rehabilitation trajectory. As such, this adds essential new information on the future use of this instrument.

In terms of administration time and level of confrontation, the CRS-ISA-DD is a feasible instrument. Assessment of the psychometric properties indicate excellent absolute agreement on both the ISA and DD scales, as reflected by the high ICC scores. This is in line with other studies that report high inter-rater reliability of the CRS-ISA-DD [8, 17]. The internal consistency was good for the ISA scale and acceptable for the DD scale. Collection of information necessary to complete the CRS-ISA-DD, such as the neuropsychological assessment and interview with patient and significant other, was time-consuming in this particular research setting. However, once all information is gathered and one is familiar with the scale, the CRS-ISA-DD can be completed within 10 minutes. Raters judged the scale as easy to use.

The patients showed overall good awareness of deficits, reflected in the low average discrepancy scores on the PCRS and the low average scores on the ISA and DD scales of the CRS-ISA-DD. Unexpectedly, PCRS discrepancy scores were not significantly correlated to ISA or DD. A possible explanation is that they measure more distinct aspects of awareness than we hypothesized. Recognizing a problem when it occurs and anticipating future problems require higher levels of awareness than merely understanding changes in one's level of functioning [42]. The PCRS is a self-report measure addressing understanding of difficulties patients are dealing with, while the CRS-ISA-DD is a clinician-rated instrument based on the patient's behavior. Besides differentiating between ISA and DD, it also includes observations of patients during tasks and can assess their reactions and awareness while making mistakes.

Participants who were more severely injured showed more severe levels of ISA while injury severity had no associations with DD. Furthermore, in line with other studies [9, 43], patients with more severe ISA performed worse on tests for processing written information, memory and planning. Injury severity has been associated with less efficient brain network functioning [44]. In turn, injury to networks such as the fronto-parietal control network have been associated with impaired self-awareness [45]. The neuropsychological tasks used in the study indicate impairments in different cognitive functions and underlying brain networks. The correlations of ISA, but not DD, with poor performance on these tasks suggest ISA is associated with neurocognitive factors while DD is not.

There was a significant negative correlation between DD and anxiety symptoms. This is in line with previous research [9] and suggests that denial of disability is a psychological mechanism to protect against emotional distress [8, 14]. No evidence for a positive association between DD and avoidance coping was found. This is possibly due to a lack of anxiety to drive the avoidance behavior. However, this finding is in contradiction to previous studies [17]. Mean avoidance coping scores were much lower in the current sample and time since injury was longer. As mentioned before, DD and avoidance behavior might be mostly present in the more acute phases following TBI. An assumption is that those who participated are generally functioning at a reasonable level in society and do not need to engage in other defense mechanisms. There is no information on societal participation (e.g. return to work/education, independent living, and supervision) in the current study. It would be interesting to take this into account in future studies.

The use of defense mechanisms was not in line with our hypotheses. Patients with more severe ISA made more use of the denial defense and less use of the projection defense relative to the other defenses, while DD was not associated with any of the defenses. It is important to note that the process of translating the TAT stories before scoring might have influenced the results. Moreover, denial is scored when patients fail to respond to certain aspects of the pictures [46]. Individuals with high ISA scores simply might not attend to all relevant stimuli or do not perceive them as threatening due to their cognitive impairments. Furthermore, defense mechanisms can be placed on a developmental continuum with denial being the most immature defense, followed by projection and then identification [46]. Since cognitive performance was more compromised in patients with more severe ISA, their ability to use more mature defenses may have been reduced as well. This is in line with findings of Cramer (2002), who found that 'cognitive weakness' was one of several behavioral correlates in the use of denial in young adults.

There was an unexpected sampling bias; only 42% of patients approached agreed to participate. ISA and, in particular, DD may be uncommon problems in chronic community-dwelling TBI populations. However, it has been shown that self-awareness problems persist into the chronic phase [47]. True prevalence of ISA and DD in community-dwelling TBI patients could be higher than detected. Individuals with higher levels of ISA and DD might have participated but might still have been unwilling to discuss their problems during assessment. Alternatively, they might have refused participation altogether since they found it too confronting or anticipated a quarrel. This is a paradox: the behavior we want to quantify is the reason that we cannot measure it. A more accurate representation ISA and DD prevalence could be detected via changing the sampling procedure. For example, potential participants could be recruited through significant others instead of through former treating physicians or psychologists. Furthermore, contacting the participants at a shorter time since injury might be beneficial to increase participation. This way, relevance for the participants themselves increases as well as the chance of enrolling patients with higher levels of DD. However, this would lead to a different patient population with more acute TBI. In order to investigate ISA and DD in a chronic community-dwelling TBI population, making the assessment procedure less confronting between patient and significant others could enhance response rates. Although it was necessary for this study to observe patients' reactions to significant others' opinions, it might help if the interviews are held separately.

A limitation of this study is that despite the considerable sample size, the final sample did not include a large variability of ISA and DD scores. Nonetheless, the results provide useful new information on measuring self-awareness in a community-dwelling TBI population. The ISA and DD scores obtained in the current study were lower than the scores in the original study of construct validation of the CRS-ISA-DD [8]. It is important to realize that the CRS-ISA-DD was developed in a clinical setting. In such setting, a clinician would decide to use the instrument after suspecting a self-awareness problem. In a community setting, such as in the current study, the patient and significant other are asked to observe their own behavior and determine whether there is a self-awareness problem. However, especially in the presence of self-awareness problems, this might be difficult, if not impossible, for them to assess. Thus, despite the feasibility of the CRS-ISA-DD, the results indicate the instrument is not very useful as a general screening instrument when administered by someone not familiar with the patient. The instrument might be more useful when awareness problems are evident and when administered by someone who is familiar with the patient. This would often be in a clinical setting. Determining which type of treatment is necessary should be done as soon as possible. Therefore, the instrument would be of great use early in the rehabilitation trajectory. However, if awareness problems persist until later in the rehabilitation trajectory, this instrument can still be effective in determining which type of awareness problems are most prominent and how to best deal with them. By conducting an initial screening and recruiting only those patients with impaired self-awareness problems, the usefulness of CRS-ISA-DD as a diagnostic tool to separate ISA from DD can be further explored.

In conclusion, despite a low variability of scores on the CRS-ISA-DD, ISA and DD seem to occur in a population of community-dwelling TBI patients. The prevalence in the current study might be an underrepresentation. Overall, the CRS-ISA-DD is a feasible instrument with excellent inter-rater reliability and acceptable-good internal consistency. The data suggests that the ISA and DD scales measure different phenomena. The ISA subscale correlates with injury severity and cognitive problems and seems to be able to distinguish unawareness of deficits as a result of a neurologically based deficiency. In the current sample, it remains unclear whether the instrument can also dissociate a DD group that correlates with psychological denial factors. The CRS-ISA-DD has potential as a diagnostic tool but the current study suggests it is less applicable as a screening tool for self-awareness problems in a community-dwelling TBI population. However, once a self-awareness problem has been identified, the instrument could be very useful to differentiate between

ISA and DD, in both the clinic and at home. For scientific purposes, it is desirable to have more variability in the ISA and DD scores in order to draw more reliable conclusions. Therefore, in future research it would be interesting to use the CRS-ISA-DD as diagnostic tool in a community-dwelling TBI patient population in which self-awareness problems have already been established.

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Appendix 1. Assessment procedure protocol

Interview

"*I have understood from your rehabilitation doctor that you have had a traumatic brain injury a while ago. For this study, I would like to know how you are doing at this moment, a while after the injury. I would like to hear your own opinion but also that of your significant other.*"

"*Do you yourself notice any changes compared to how you were doing before you got the brain injury?*"

"*Now I would like to hear the opinion of your significant other. It could be the case that he or she has a different opinion. That does not mean either of you is wrong. I would just like see whether you have different opinions.*"

Ask significant other: "*What is your opinion? Do you notice any changes, or do you think he or she has any difficulties?*"

Repeat wat significant other says:
"*Your significant other says '...'. What do you think of that?*"
Compare opinions for every problem mentioned. Also observe whether patient is easily agitated or understanding. Observe the significant other too. Does he/she seem agitated by the answers the patient is giving?

In case both patient and significant other do not mention any problems:
"*Other people sometimes tell me that they have trouble remembering appointments or names / became slower or things are going too fast for them / are agitated more easily or faster than before / can't do their job or hobby's anymore. Do you notice any changes in this?*"

Also ask if someone previously had trouble admitting to mistakes, and whether that has changed?

Ask whether significant other has anything to add.

"Okay. Now I would like to talk about some other things. I am going to ask you some general questions."

"What is your age?"

____

"What kind of education have you had?"

____

____

"What kind of job do/did you have?"

____

____

"Can you tell me something about your family situation? Are you married? Do you have children?"

____

____

"How is your sleeping going? Do you fall asleep easily? Do you wake up often? When you wake up, can you fall asleep easily again afterwards? What time do you go to bed? What time do you wake up? Is this different from before?"

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"Do you dream a lot? Is this different from before?"

____

____

"How is your appetite? Do you notice changes in your appetite, or did you gain or lose weight?"

____

____

"*How is your sense of taste/smell?*"

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____

"*How is your muscle strength? Do you notice any changes in the strength of your arms or legs?*"

____

____

"*Do you smoke?*"

____

"*Do you drink alcohol? What do you drink? How much/often?*"

____

Ask whether significant other has anything to add.

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These questions take away the tension and give an impression of reliability of the participant.

"*Now I would like to hear your opinion on how difficult certain things are for you. I am going to ask for specific things. Perhaps you might experience some things as more difficult than before, perhaps you do not experience difficulties at all. I would like to ask you answer each question with a score between 0 and 10. 0 means you do not experience any difficulties, 10 means serious difficulties. The smaller the number, the smaller the difficulty.*" First ask the patient for a score and then ask the significant other.

– "*When it comes to your everyday memory, things you find important to remember, how difficult is that for you on a scale from 0 to 10? 0 means you do not find it difficult, 10 means you find it very difficult.*" __________________

– "*When it comes to attention or concentration, holding your attention when there is noise or other distraction. How difficult is that for you? 0 means you do not find it difficult, 10 means you find it very difficult.*" __________________

- *"When it comes to finding the right words, words that you want to use to say something, how difficult is that for you? 0 means you can do it easily, 10 means you have serious difficulties finding the right words."* ____________________
- *"When it comes to irritability, getting angry about small things, even if you do not show it? 0 means you are generally quiet and calm, 10 means you can get annoyed by the smallest things."*____________________
- *"Are you ever anxious or do you worry? This could have a clear reason but the reason for this could also be more unclear. 0 = I am generally calm, 10 = I am so upset that it influences my daily functioning"*____________________
- *"How is your mood? 0 = my mood is normal, you have good days and bad days, but you have a positive view on life, 10 = I feel sad and sometime feel it's not worth living."* ____________________
- *"When it comes to fatigue, having the energy to do what you want to do. 0 means you generally have the energy to do what you want to do. 10 means you are fatigued quite fast and cannot always do what you want to do."*

  ____
- *"How is your coordination, getting lost in spaces, for example being able to find your car after being in a shopping mall for 2 hours? 0 means you have no difficulty with this, 10 means you experience serious problems, for example that you have no clue where you parked your car."*____________________

Ask whether significant other has anything to add.

____

____

____

Neuropsychological tests

"Now I would like to ask you to do a few tasks so that I can create my own opinion on whether certain things might be difficult for you. Some tasks are easy, and others are difficult. Nobody can flawlessly complete them all. Just try to do your best. While you are doing the tasks, I would like to ask your significant other to fill out a questionnaire. Later, I will also ask you to fill out the same questionnaire."

Ask the significant other to fill out the questionnaire, PCRS, in another room so the patient is not distracted during the tasks.

Do the following tasks:

- Thematic apperception test (TAT)
- Phonemic fluency
- Zoo map Test
- Visual Verbal Learning Test (VVLT)
- The Letter Digit Substitution Test (LDST)
- Halstead Finger Tapping Test (HFTT)
- Visual Verbal Learning Test (VVLT) - delayed recall
- Block Design Test

Pay attention to effort, comments during the tasks ("stupid, this means nothing"), self-monitoring of performance, appearance and personal hygiene.

Observations of researcher during the neuropsychological tests:

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"*Thank you very much for your effort. How did it go?*"

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Give feedback on the VVLT, LDST and Block design tasks:
"*I had the impression that … was a bit difficult for you. On average people score …, you scored …*" Show how the patient scored, use one of the tests that were difficult. "*How did you experience this?*" Pay attention to the patient's reaction.

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Observations of researcher during feedback on tests:

Questionnaires

"*Finally, I would like to ask you to fill out some questionnaires.*"

Let the patient fill out the following questionnaires:

- Patient Competency Rating scale (PCRS)
- Hospital Anxiety and Depression Scale (HADS)
- COPE inventory

CRS-ISA-DD

Based on the interview and observations during neuropsychological testing and feedback, score behaviors on the CRS-ISA-DD.

Appendix 2. CRS-ISA-DD (Revision December 2013)

Clinician Rating Scale for Evaluating Impaired Self-Awareness and Denial of Disability (CRS-ISA-DD)

George P. Prigatano, PhD, and Pamela S. Klonoff, PhD
Revised December 2013
Patient's name: **Date of Birth:** **Assessment Date:**

5

ISA scale		
		Y N S 0-10
1	In response to general questions, patient spontaneously reports few, if any neuropsychological problems since the onset of their brain injury. If they report problems they will often be of physical nature.	
2	In response to specific questions, patient states they have no problems, or if 'some' problem is partially recognized the patient perceives the problem as less severe than what relatives report or what neuropsychological tests indicate.	
3	Patients show little affective reaction or react indifferent to hearing feedback from a significant other and/or professional that they may have more difficulties than what they report.	
4	Patient appears perplexed or may look at you confused when receiving feedback from a significant other and/or professional that they may have more difficulties than what they report. [note: patient eventually can get angry if you keep pushing because they do not notice any problems]	
5	When there is a discrepancy in the patients' perceptions versus relatives' and/or professionals' perceptions the patient does not provide an (logical) argument for his or her point-of-view when asked about the discrepancy.	
6	Patient does not appear to recognize the interpersonal or social impact of an impairment.	
7	Based on performance on neuropsychological tests and behavior during testing (which can also be supported by a relative's statements), the patient often demonstrates behavioral characteristics indicative of problems of initiation, self-monitoring (e.g., disinhibition, socially inappropriate comments, lack of personal hygiene), planning, and other 'higher cerebral functions' often considered mediated by frontal-limbic systems of the brain.	
8	A reliable significant other notes that the patient does not seem to fully recognize a clear behavioral difficulty. This may be a spontaneous comment or elicited upon questioning. The point is that the reliable other often states that the patient does not seem to fully understand what is wrong despite feedback from them and the passage of time.	
9	Patients may have problems in performing unstructured tasks (e.g., initiating behavior and monitoring their behavioral performance), but are able to work on a task when given structure or are told what to do step by step.	
10	Patient demonstrates a 'cognitive perplexity' (appears stunned or confused about their inability to perform a task) and/or no emotional reaction when they cannot solve various neuropsychological tasks during testing and/or rehabilitation. Is generally slow and calm during tasks and interview.	
	Total score ISA scale:	

Y=Yes; N=No; S=Severity

DD scale					
		Y	N	S 0-10	
1	In response to a general question, patient spontaneously reports noticing some possible change in their abilities, but has a difficult time defining exactly what those changes may be. The patient's description is often vague and it is difficult to evaluate whether or not the patient sees it as an important problem in their life.				
2	Patient may admit, upon specific questioning, to disturbances in higher cerebral functioning, but are quick to add that deficits or impairments are not important or have no substantial impact on their day-to-day life.				
3	Patient shows a negative affective reaction when given feedback that they may be more impaired than what they report (e.g., tone of irritation, rolling of eyes, quick to dismiss the feedback) or tries to repress the problem (stating that they do not want to talk about it or have already talked about it).				
4	Patient does not appear perplexed when hearing a relatives' or significant other's feedback, but counters their statement with either evidence or quickly dismisses their points of view as to why they are incorrect.				
5	When the patient attempts to give an argument for their point-of-view, there is a thread of logic to it (excuses could be plausible) but salient points may be missing. Or patient argues why it is not their fault when something goes wrong.				
6	Significant other notes that premorbid the individual had a difficult time admitting to difficulties (patient would never either admit to mistakes or consider themselves wrong in their decisions). This behavior does not seem to be significantly changed from premorbid status.				
7	Reliable significant other notes that the patient provides excuses for failures despite repeated feedback and the passage of time.				
8	The patient may demonstrate no or mild difficulties with initiation, planning, or monitoring their performance while taking neuropsychological tests. They are typically not severely impaired in these areas.				
9	When undergoing neuropsychological testing, patients are prone to make sarcastic or negative comments about the usefulness of neuropsychological tests and their ecological validity.				
10	Within the context of a neuropsychological examination or rehabilitation activity, the patient is often easily upset when faced with a behavioral failure. They frequently have explanations as to why they do poorly on certain tests and discount the role of their brain injury.				
	Total score DD scale:				

Y=Yes; N=No; S=Severity

Summary DD scale
Total 'Yes' score:
Total 'Severity' score

Summary ISA scale
Total 'Yes' score:
Total 'Severity' score

CHAPTER 6

Socratic Guided Feedback Therapy after Acquired Brain Injury: a Multicenter Randomized Controlled Trial to Evaluate Effects on Impaired Self-Awareness

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CHAPTER 7

General discussion

General discussion

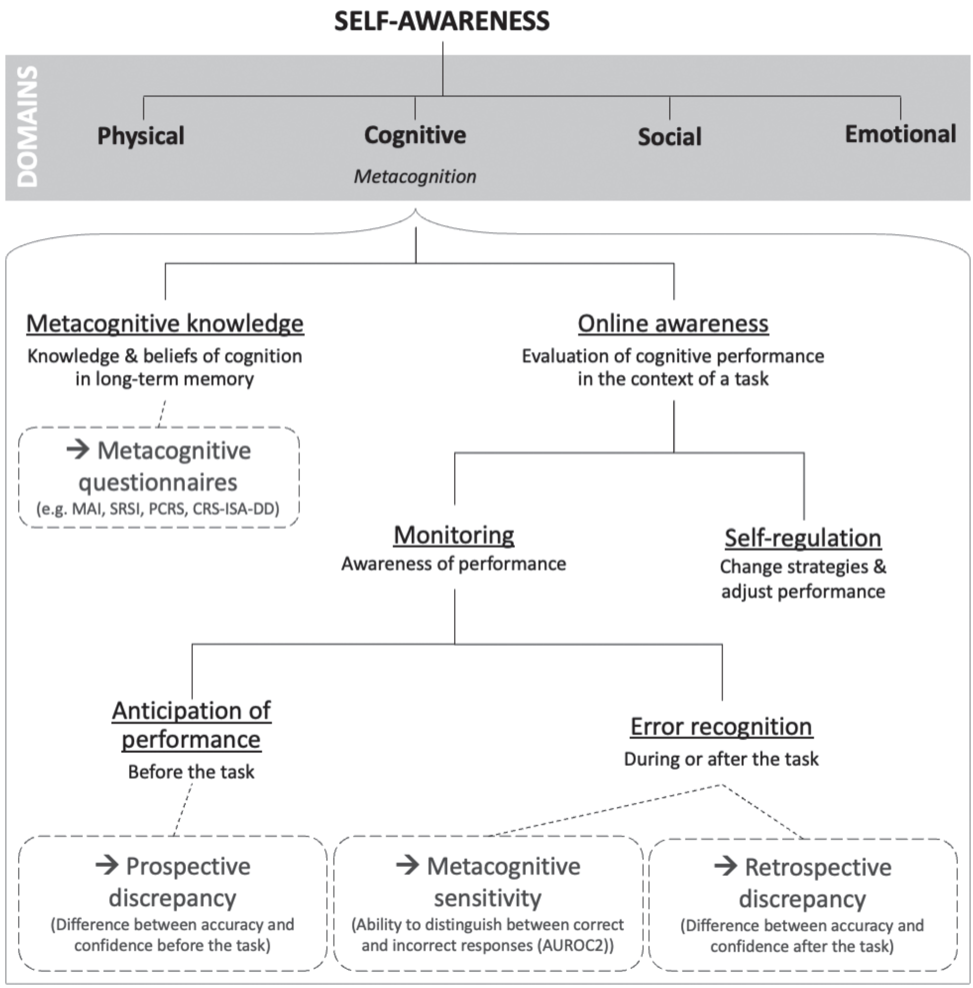
The aim of this thesis was to contribute to the understanding, measurement, and treatment of impaired self-awareness after ABI. Impaired self-awareness is an important factor in rehabilitation treatment after ABI [1] as it is associated with poor treatment adherence [2-5], poor rehabilitation outcomes [6-11], and high burden on relatives [12, 13]. We investigated the elements that self-awareness consist of and how these relate to psychological, cognitive, and neural factors. Additionally, a new intervention for treating impaired self-awareness was investigated. In the current chapter, we discuss and reflect on the main findings in light of the four research questions presented in chapter 1, followed by suggestions for future directions, clinical implications, and concluding remarks. As represented in figure 1, self-awareness is an umbrella term that describes awareness of one's functioning in any domain, such as the physical, cognitive, social, or emotional domain [10]. The studies in this thesis particularly focused on self-awareness of the cognitive domain, which is also called metacognition [14]. Both terms are used throughout this thesis, metacognition when specifically referring to self-awareness in the cognitive domain and self-awareness when referring to the broader concept of awareness of one's behavior.

Main findings and implications

Measuring elements of self-awareness

Figure 1 depicts the overview of the different elements of self-awareness which will serve as a framework for this discussion. Metacognition is a broad term and falls within the cognitive domain of the even broader term self-awareness. On the one hand, offline metacognitive knowledge is knowledge and beliefs of cognition stored in long-term memory [15]. This is typically measured using questionnaires. Some questionnaires quantify metacognitive knowledge of cognition specifically, such as the Metacognitive Awareness Inventory (MAI) [16], while others concern metacognitive knowledge across several domains (e.g. cognition, behavior and emotions), such as the Patient Competency Rating Scale (PCRS) [17]. Online awareness, on the other hand, is evaluation of cognitive performance in the context of a task [15]. This branches out into monitoring and self-regulation. Monitoring further branches out into evaluation before, during, or after a task. Monitoring can be measured using metacognitive sensitivity measures or discrepancy scores between accuracy and either prospective or retrospective confidence judgments [18].

Figure 1. Overview of the elements of self-awareness.



Note. In the dashed boxes are measurement methods employed in this thesis. PCRS = Patient Competency Rating Scale. SRSI = Self-Regulation Skills Interview. CRS-ISA-DD = Clinician's Rating Scale for Evaluating Impaired Self-Awareness and Denial of Disability. MAI = Metacognitive Awareness Inventory. AUROC2 = area under the type 2 receiver operating characteristic curve.

Measuring metacognition in healthy subjects

To investigate whether these elements are actually separable distinct elements or highly correlated elements, we investigated the associations between the elements in a sample of young healthy people in chapter 2. We found a clear association between metacognitive sensitivity and both prospective and retrospective discrepancy scores. No direct association was found between metacognitive sensitivity and metacognitive knowledge in our study. These results fit in the neuropsychological as well as educational literature that distinguish online from offline components of metacognition [19]. This lack of association between online and offline measures is important because it means that status of one element of metacognition cannot be inferred by measuring another element of metacognition. Instead, the specific element of interest must be measured directly. For example, information about metacognitive knowledge measured with questionnaires cannot be used to infer information about online awareness during tasks.

Measuring impaired self-awareness in ABI patients

Translating the results from chapter 2 to self-awareness after ABI implies that an impairment in a certain element of self-awareness can only be determined if the specific element is measured directly. Although this sounds very straightforward, research and the clinic commonly assess self-awareness on the level of metacognitive knowledge only [17]. However, results cannot be generalized to elements of online awareness. Our results indicate that not just one element should be measured to infer an overall level of self-awareness. Instead, it is important to be clear on what element of self-awareness should be quantified and to choose the measurement method accordingly.

There is another important aspect to impaired self-awareness to take into account. Namely, different underlying mechanisms may cause a reduction in self-awareness. This reduction could be due to neurocognitive factors such as disrupted brain network functioning [20] or psychological factors or coping mechanisms such as denial [21]. To this end, in chapter 5, we investigated whether the Clinician's Rating Scale for Evaluating Impaired Self-Awareness and Denial of Disability (CRS-ISA-DD) [22] is a reliable and feasible instrument that can be used to differentiate impaired self-awareness as a neurocognitive deficit (ISA) from denial of disability (DD). This instrument can be placed at the level of online awareness, in particular self-regulation, as clinicians or researchers observe a person's behavioral reaction to mistakes and feedback. The results showed that the two scales (ISA and DD) of the CRS-ISA-DD correlated with different neuropsychological measures: ISA severity correlated with neuropsychological test scores and injury severity, while DD severity correlated with anxiety. This suggests that there are indeed different mechanisms that could lead to reduced self-awareness and fits the biopsychosocial approach that has been suggested in previous literature well [23]. Both clinicians and researchers should be aware of the different origins of reduced self-awareness as this information is necessary to advance models of self-awareness as well as tailor treatment to individual needs.

In chapter 5 we further saw that when administering the CRS-ISA-DD to a community-dwelling population of people with TBI, most participants showed one or more symptoms of ISA (73%) and DD (74%). However, this was often of low severity. Important to keep in mind is that only 42% of individuals who were approached to participate, eventually consented to participate in the study. Therefore, it is hard to say how often ISA and DD truly occur. This low, and likely biased, response rate reveals the paradox of doing research into reduced self-awareness: the behavior we want to quantify is the reason that we cannot measure it. Someone with impaired self-awareness, who does not want to or who cannot reflect on their behavior, will likely pass on participation in such studies. The same is true for significant others who want to avoid conflict with the person with reduced self-awareness.

Neural correlates of metacognition in ABI patients and healthy subjects: an integration

In chapter 4, we systematically reviewed the literature on the neural correlates of impaired self-awareness after ABI. The results were categorized based on measurement method. This classification was also used for the fMRI study in chapter 3 and fit our model in figure 1. In chapter 3, we investigated brain activity while healthy subjects were making confidence judgments while performing cognitive tasks and compared metacognitive accurate and inaccurate judgments. People indicated how confident they were that their answer in a memory task was correct. Essentially, we compared brain activity between trials in which the confidence judgment was justified (e.g. high confidence for correct answers) to trials when the confidence judgment was unjustified (e.g. low confidence for correct answers). The latter is representative of reduced metacognition. We will discuss the results of these two chapters per element of metacognition.

Metacognitive knowledge

In chapter 3, the difference in brain activation between high and low confidence trials was correlated with scores on questionnaires of metacognitive knowledge.

In doing so, we found indications that the knowledge of cognition subscale of the Metacognitive Awareness Inventory [16] is associated with the left middle frontal gyrus activity and that the regulation of cognition subscale is associated with activity in the right insula. In our systematic review, we found that more impaired self-awareness after ABI (i.e. higher self-proxy discrepancy scores on questionnaires) is associated with frontal lobe damage, decreased task-related activation in the right frontal lobe, as well as higher mean diffusivity in the whole white matter of the brain (chapter 4). These studies together imply that the frontal lobes are involved in metacognitive knowledge. This is in line with the fact that the frontal lobes are involved in executive functions such as memory retrieval, decision-making, understanding social behavior, and manipulation of information in working memory [24-26]. These are all necessary functions to properly fill out these metacognitive knowledge questionnaires, as they require an integration of knowledge and beliefs of cognition in a certain context and timeframe (e.g. assess how difficult it is to behave appropriately when you are with friends). Furthermore, we found indications that the right insula is associated with the regulation of cognition subscale of the Metacognitive Awareness Inventory [16] in the healthy participants (chapter 3).

Self-regulation

In chapter 4 we found that after ABI, the anterior cingulate cortex (ACC), frontal gyrus, left insula, and parietal operculum are associated with self-regulation as measured by implicit self-awareness tasks. For these tasks, participants needed adequate self-awareness (i.e. knowing whether their answer was correct or incorrect) in order to perform well. For example, in a stop-signal task in which mistakes have to be corrected [27]. Overall, self-regulation seems to be associated with the salience network, which consists of temporal poles, insula, and ACC [28]. This network is involved in detecting relevant stimuli and preparing to respond to these stimuli, which is necessary to regulate one’s behavior [29].

Monitoring

In chapter 4, we found that recognition of mistakes in ABI patients with impaired self-awareness is associated with more internetwork connectivity of anterior or posterior default mode network (DMN) to salience network [30]. We went on to investigate brain activity in these networks in healthy subjects while doing a metacognitive task (chapter 3). Results show indications that the anterior DMN (middle frontal gyrus and superior frontal gyrus), precuneus, and insula are more active while making confidence judgments when the confidence judgment was justified (e.g. high confidence for correct answers) than when the judgment was unjustified (e.g. low confidence for correct answers). While the studies in the systematic review often compare between people, from the experimental study we now have preliminary evidence that there is also some distinction of metacognitive accuracy on a neural level within persons.

Overall, these results indicate that the different elements of metacognition are at least somewhat separable on a neural level too. Different brain networks seem to be involved in the different aspects of metacognition. This information can be used to further develop understanding of the different constructs and help build theoretical models, which can support better measurement and, ultimately, can support treatment development.

Improving self-awareness in ABI patients

All the studies in this thesis were conducted with one ultimate goal, to improve rehabilitation for people with impaired self-awareness after ABI. In that sense, chapter 6 describes the grand study of this thesis. It is the most substantial study in terms of clinical necessity as well as laboriousness. In chapter 6, we report on a multicenter randomized controlled trial in which we investigated the effectiveness of a new treatment, Socratic Guided Feedback therapy, on improving self-awareness and other rehabilitation outcomes (i.e. motivation for and participation in therapy, mood, quality of life, and social participation). The new treatment was compared to care as usual and results show that self-awareness improved over time regardless of treatment group. We can conclude that the Socratic Guided Feedback treatment is as good as care as usual but we found no additional effects, except for a possible positive late effect of the treatment on one of the self-awareness measures. Namely, the PCRS discrepancy score between patient and significant other decreased in the experimental intervention group (indicating better self-awareness) while it increased in the care as usual group between 9 and 12 months after baseline measurement. It is plausible that the effects of the treatment only come to light as people have had sufficient time back in their usual routine at home to self-discover the limits of their recovery [31]. To further investigate this late effect, it would be interesting to have more follow-up measurements that stretch beyond one year after the baseline measurement.

A possible reason for not finding beneficial effects of the new treatment compared to care as usual is that the intervention and outcome measures do not target the same elements of self-awareness. The Socratic Guided Feedback therapy is aimed at self-reflection and monitoring. The measurements used to quantify self-awareness in the study in chapter 6 were the Self-Regulation Skills Interview (SRSI), a semi-structured interview in which the researcher rates the interviewee [32], and the PCRS, a self-report and informant-reported questionnaire [17]. These can both be classified as metacognitive knowledge measures in figure 1. Thus, the measurement instruments used do not target the same elements of self-awareness as the treatment does. Theoretical foundations on how or why an intervention would work are crucial [33]. Evaluating this intervention in the current theoretical model of figure 1, the misalignment between intervention targets and outcomes measured could explain the lack of positive effects of the intervention. It would be interesting to investigate the effects of the Socratic Guided Feedback intervention on outcomes measured on the level of monitoring and self-reflection.

Extending this to neurocognitive impaired self-awareness (ISA) and psychological denial of disability (DD), these two types of impaired self-awareness might require different treatments and measurement methods. As was shown in chapter 5, a distinction can be made between ISA and DD but this distinction cannot be made with the measurement instruments used in chapter 6. It could be the case that Socratic Guided Feedback therapy is more effective in one of the two types. Individuals with high levels of denial have resistant and angry reactions when confronted with their impairments [34]. This confrontation is avoided in the Socratic Guided Feedback therapy and, therefore, treatment effects might be stronger in people with predominantly DD. However, we saw in chapter 5 that this group is not likely to participate in such studies. Therefore, the majority of the group likely had predominantly ISA, which could have diluted the effect on the group with predominantly DD.

The Socratic Guided Feedback therapy might not affect self-awareness directly but might influence other factors in the therapy room that can make the therapy less confronting and, therefore, potentially more effective. An essential element of the therapy is understanding each other and communication. If there is less confrontation, there might be less conflict, which in turn may lead to better treatment adherence and better outcomes. In a review on Motivational Interviewing, which is a similar approach, it has indeed been suggested that adopting a more client-centered therapeutic style builds a positive alliance between patient and rehabilitation team, which would then enforce engagement in rehabilitation [35]. Therefore, other moderating factors should be considered such as therapeutic alliance [36]. In addition, brain injury can have a significant effect on partner relationships [37]. Helping partners understand this Socratic Guided Feedback approach could help them in their communication with their loved one while, simultaneously, possibly increasing effect of the therapy. Therefore, another important outcome measure to consider is caregiver burden [38].

The Socratic Guided Feedback therapy might be more effective when delivered more frequently and in multiple contexts. Firstly, the intervention tries to establish behavioral modification, which might need more intense delivery than can be achieved during cognitive therapy alone. This essential therapeutic attitude should be maintained persistently by everyone in the patient's environment to strengthen the improvement in self-awareness. This includes all therapists around the patient, patients around each other, and the social environment around the patient at home. Secondly, environment and social influence is one of the five key themes in behavior change [39]. Within this theme, research shows that learning new behavior is context-dependent, which would advocate for involving as many contexts as possible. This would entail the different disciplines in the rehabilitation setting but also including social contacts in the community such as relatives, friends, and employers. Thirdly, according to self-determination theory, the three key factors for enlarging intrinsic motivation, which is necessary for rehabilitation, are competence, relatedness, and autonomy [40]. A safe environment in which someone feels valued can enforce these three factors, while an opposite environment can have deleterious effects [40]. In that sense, it is also important to create a sense of trust and connectedness, which could be achieved by offering the therapy in group therapy settings and including caregivers.

Overall, chapter 6 confirms that self-awareness improves after cognitive rehabilitation, as has been shown in other studies [41-43]. Alternatively, this improvement could be the course of natural recovery. The natural course of recovery of impaired self-awareness after ABI without rehabilitation is unknown because such studies would entail unethical study designs that withhold patients from treatment. Unfortunately, the clinical issue presented at the start of this thesis, the difficulty of treating impaired self-awareness, has not completely been solved yet. Therefore, it is important to continue investigating which therapy helps best. To do so we must, on the one hand, offer treatment in multiple contexts as described before and, on the other hand, critically assess where we expect to gain the most, which aspects of self-awareness are targeted, and how these outcomes are best measured.

Strengths and methodological considerations

A strength of this thesis is that we tried to improve the way of quantifying self-awareness and, more specifically, metacognition. This was done by breaking down metacognition into different elements and measuring them in different ways. All studies in this thesis investigated these elements separately, which allows the results to fit into the theoretical structure presented in figure 1. As self-awareness is an umbrella term covering broad concepts, braking self-awareness down into different elements makes it more tangible. Specifying which element is targeted or measured will allow better comparison of studies. This will help further development of theoretical models and future studies that investigate these topics. Furthermore, we used research methods across the board, ranging from more fundamental and theoretical studies to clinical trials. We have used questionnaires, tasks, structured interviews, psychological correlates, neural correlates, systematically reviewed existing literature, and have investigated this in healthy subjects as well as in people with ABI. Overall, we have been able to add some pieces to the puzzle but have, perhaps more importantly, identified how to do so most efficiently.

There are some methodological considerations to take into account. Firstly, the healthy subjects included in the studies are mostly young university students. This is not an average person and, thus, not generalizable and not comparable to the ABI populations in the studies in this thesis. Future studies should replicate the studies in chapter 2 and 3 in ABI populations and control groups. These studies provide a feasible framework that can be easily implemented in future studies. Secondly, many instruments can only measure self-awareness indirectly. Clinician ratings, self-proxy discrepancy ratings, and structured interviews always depend on someone’s opinion, which will always have the risk of being biased. Tasks, on the other hand, are more objective but have drawbacks such as poor ecological validity.

Future directions

It is important to assess the different aspects of self-awareness properly and to offer treatment accordingly. To do so, future research should further develop theoretical models and measurement instruments to assess the different elements of self-awareness. It is important that studies clearly operationalize what element of self-awareness they are measuring in order to facilitate comparison between studies. Research into the treatment of impaired self-awareness should have clear theoretical foundations [44]. These should also operationalize what element of self-awareness they are targeting and use outcome measures that match this. In the different studies throughout this thesis, it became clear that there is a variability in level of self-awareness between people. A next step is to investigate which factors can determine or influence this. As has been shown in chapter 5, denial and neurocognitive impairments are two pathways that could lead to impaired self-awareness. Future studies should pay more attention to the underlying mechanisms of impaired aspects of self-awareness and therapeutic implications. The study in chapter 3 provides a feasible set-up to investigate neural correlates of metacognition in young healthy subjects. Future studies should investigate brain activity during such tasks in people with ABI and controls. This would add to the understanding of the neural processes involved in metacognition and how an ABI affects this. Finally, significant others should be involved when measuring the effectiveness of treatment but also in the interventions themselves. This could be an area where there is a lot to gain. Caregivers should be given more tools to cope with impaired self-awareness of individuals with ABI in order to reduce friction. Qualitative studies could help understand what the biggest struggles are in the therapy room but also at home. This should be done taking into account the different perspectives of patients, significant others, caregivers, and therapists.

Clinical implications

Self-awareness is an umbrella term under which there are several elements. These cannot be measured with one global measurement instrument. Instead, the elements of interest should be identified and measured directly after having specified in which domain the impairment is. Additionally, it is important to identify why a certain element of self-awareness is reduced or impaired. This could be due to, for example, neurocognitive factors or psychological factors, which can be measured using the Clinician's Rating Scale for evaluating Impaired

Self-Awareness and Denial of Disability (CRS-ISA-DD). We recommend using this instrument as diagnostic tool to identify the origin of self-awareness problems once reduced self-awareness has been identified. Treatment can then be tailored to suit the element of metacognition that is reduced and the underlying cause. For example, whether cognitive therapy or psychological therapy should be indicated. Furthermore, we recommend using the Socratic Guided Feedback therapy when treating ABI patients with impaired self-awareness. This feasible treatment is as effective as care as usual and offers structure to therapists, which could be extended to significant others.

Concluding remarks

This thesis confirms it is difficult to get a grasp on self-awareness. Despite several null findings, a lot has been learned along the way. First, the results of this thesis show that there are many ways to measure self-awareness depending on how you define it. There are distinguishable elements of self-awareness. Second, results show that the different elements seem to be related to different brain networks. With these studies, we provide tools on how this can be further investigated in a structured way. Third, impaired self-awareness after ABI improves when individuals receive rehabilitation treatment. The Socratic Guided Feedback treatment is as effective as care as usual and possible additional effects may still be hidden. Therefore, it can be seen as alternative to care as usual. Overall, it has become clear that it is important to be specific about which element of self-awareness one is interested in, measure that element properly, and tailor treatment accordingly. An important lesson learned is that we should approach studying self-awareness like eating an elephant: one bite at a time.

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ADDENDUM

Summary

Nederlandse samenvatting
(Dutch summary)

Impact paragraph

Curriculum vitae

Acknowledgements (dankwoord)

SUMMARY

Summary

Self-awareness is one of the most important factors contributing to the success of rehabilitation treatment after acquired brain injury (ABI). Self-awareness refers to the ability to reflect on your own behavior. Unfortunately, many individuals with ABI can suffer from impaired self-awareness. This means it is difficult for them to understand the consequences of their injury and the effects these have on themselves and their surroundings. This is associated with poor treatment adherence, poor rehabilitation outcomes, and high burden on caregivers. If we say self-awareness is a cognitive function that is impaired after brain injury, there is an implicit assumption that unimpaired self-awareness also exists. Self-awareness is an umbrella term that refers to awareness of one's functioning in any domain, such as the physical, cognitive, or emotional domain. Self-awareness of the cognitive domain is also called metacognition. Therefore, both terms are used in this thesis. Impaired self-awareness is a very important clinical issue but evidence-based treatments are lacking. This is partly because it is unclear what self-awareness is conceptually and how impairments in self-awareness are caused. Self-awareness is difficult to grasp and there are different models describing the concept. It is a broad term covering a range of behavioral domains and it is possibly caused by multiple underlying factors.

The aim of this thesis was to contribute to the understanding, measurement, and treatment of impaired self-awareness after ABI. We investigated metacognition in people without ABI and identified the different elements it consists of. Next, brain areas that are associated with metacognition were identified. In the other studies presented in this thesis, self-awareness in people with ABI was investigated. We systematically reviewed studies to identify brain areas that are associated with impaired self-awareness after ABI, studied the nature and severity of impaired self-awareness following traumatic brain injury, assessed psychometric properties of an instrument to assess impaired self-awareness, and evaluated the effectiveness of Socratic Guided Feedback therapy as a treatment to improve impaired self-awareness after ABI.

In chapter 2, we provide an overview of the different elements of metacognition and how to measure them. Metacognition consists of two main elements: metacognitive knowledge and online awareness. Online awareness also consists of two elements: anticipation of performance and error recognition. In this study

we investigated to what extent these different elements are associated with each other. There were 128 healthy participants who filled out a questionnaire measuring metacognitive knowledge and did two cognitive tasks that allowed us to measure the different elements of online awareness. We found that the scores on the different elements of metacognition were normally distributed. This means that there are large individual differences: the scores ranged from the lower to the upper end, with most people scoring roughly in the middle. The offline measures of metacognition were not associated with the online measures of metacognition. However, the offline measures were associated with each other, as were the online measures. This indicates a clear distinction of offline versus online elements of metacognition and this should be taken into account in further research as well as the clinic. Self-awareness is a broad concept and cannot be measured with one global instrument. Instead, the separate elements should be measured directly.

Chapter 3 describes a study in which we investigated activity of certain brain networks during a metacognitive task. These brain networks were the anterior and posterior default mode network and the salience network. Forty-two healthy participants did a memory recognition task while their brain activity was recorded in an MRI scanner. The memory task was adapted so that after each trial, participants had to indicate how confident they were that their answer was correct. Brain activation during this confidence judgment was analyzed. The trials in which the confidence judgment was in line with the accuracy of their answer (e.g. they indicated high confidence for correct answers) was compared to trials in which it was not (e.g. they indicated high confidence for incorrect answers). We found indications that the left middle frontal gyrus, superior frontal gyrus, precuneus, and right insula were more active during confidence judgments when they were in line with accuracy than when they were not. As a next step, this difference in activity between the two types of trials was correlated with the different elements of metacognition. We found indications that brain activity in the middle frontal gyrus was associated with knowledge of cognition and brain activity in the insula was associated with regulation of cognition (both elements of offline metacognition). There were no correlations with an online measure of metacognition (AUROC2). These findings suggest that the different elements of metacognition are not only separable on a behavioral level (chapter 2) but also on a neural level. Different brain networks seem to be involved in the different aspects of metacognition.

To identify the neural correlates of self-awareness after ABI, a systematic review was conducted that is presented in chapter 4. After an extensive literature search, eight studies were found on the topic. These were difficult to synthesize as they used a variety of measurement methods that were not directly comparable. Therefore, the results of the studies were classified according to method of assessment. The results indicated that poor anticipation of future problems was associated with brain damage in the right frontal lobe, as well as increased diffusivity throughout the white matter of the brain. Poor performance on (self-regulation) tasks in which metacognition was implicitly measured by evaluating behavioral adjustment was associated with less functional connectivity from the fronto-parietal control network to anterior cingulate cortex and inferior frontal gyri. There was also more activation in the left insula and left parietal operculum. Worse recognition of errors was associated with less internetwork connectivity of default mode network to salience network in the brain injury group, while this association was opposite in the healthy control group. In conclusion, after ABI, differences in brain activation and connectivity are found depending on level of metacognition measured.

The nature and severity of impaired self-awareness (ISA) and denial of disability (DD) in a community-dwelling traumatic brain injury (TBI) population was investigated in chapter 5. This was done using the Clinician's Rating Scale for evaluating Impaired Self-Awareness and Denial of Disability after brain injury (CRS-ISA-DD). Additionally, psychometric properties of the instrument were assessed. Only forty-two percent (42%) of individuals approached consented to participate in this study. This illustrates the difficulty of studying topics such as impaired self-awareness and denial. Most participants who joined the study showed at least one symptom of ISA and DD, but the severity scores were low. The ISA severity scores correlated with neuropsychological test scores and injury severity, while DD severity scores correlated with anxiety. This indicates that the two constructs might have different underlying causes that require different treatments. Psychometric evaluation of the instrument showed that the CRS-ISA-DD takes less than 10 minutes to complete and is a reliable and feasible instrument. We recommend using it as diagnostic tool to differentiate between ISA and DD once self-awareness problems after brain injury have been identified.

A new treatment aimed at improving impaired self-awareness after ABI was developed and its effectiveness was evaluated in chapter 6. The Socratic Guided Feedback therapy consists of Socratic guided discussion, practicing tasks, and psychoeducation. This approach had been proven feasible and effective in previous single-case experimental design studies with four patients. In the current larger multicenter randomized controlled trial study with 64 ABI patients who had reduced self-awareness, the new intervention was compared to care as usual. Objectives were to study effects on self-awareness as well as motivation for and participation in therapy, mood, quality of life, and social participation in the long term. We found that self-awareness increased over time in both groups. Only between 9 and 12 months we found a difference between groups: self-awareness (measured by PCRS patient-significant other discrepancy score) improved in the Socratic Guided Feedback group and deteriorated in the care as usual group. No significant differences were found on the other outcome measures. We concluded that Socratic Guided Feedback therapy is as effective as care as usual, but that future research may show larger effects when fellow patients and significant others are closely involved in cognitive therapy. The Socratic Guided Feedback therapy can be considered as alternative to care as usual because the protocol provides a structure for therapists on how to deal with patients with impaired self-awareness after ABI.

Chapter 7 contains the general discussion of this thesis. The main findings are integrated and methodological considerations are discussed. Additionally, we describe implications for the clinic as well as future research. The findings in this thesis show that metacognition consists of several distinguishable elements. These elements can be measured with different measurement methods and seem to be related to different brain networks. Impairments in self-awareness can arise through different pathways. For example, they can have neurocognitive or psychological origins. The origins can be detected using the Clinician's Rating Scale for evaluating Impaired Self-Awareness and Denial of Disability (CRS-ISA-DD), which can be used to help determine which treatment should be given. The Socratic Guided Feedback treatment is an alternative treatment to care as usual. It is as effective in terms of increasing self-awareness after ABI, and possible additional effects may still be hidden. Overall, it has become clear that it is important to be specific about which element of self-awareness one is interested in, measure that element properly, and tailor treatment accordingly. We provide tools on how this can be further investigated in a structured way. An important lesson learned is that we should approach studying self-awareness like eating an elephant: one bite at a time.

NEDERLANDSE SAMENVATTING (DUTCH SUMMARY)

Nederlandse samenvatting (Dutch summary)

Inzicht in eigen functioneren is een van de belangrijkste factoren die bijdragen aan het succes van revalidatiebehandeling na niet aangeboren hersenletsel (NAH). Met inzicht bedoelen we het vermogen om na te denken over het eigen gedrag. Helaas hebben veel mensen met NAH verminderd ziekte-inzicht. Dit betekent dat zij de gevolgen van hun letsel en de effecten daarvan op henzelf en hun omgeving niet goed begrijpen. Dit hangt samen met slechte therapietrouw, slechte revalidatieresultaten en een grote belasting voor zorgverleners en naasten. Als we zeggen dat inzicht een cognitieve functie is die is verminderd door een hersenletsel, is er een impliciete aanname dat er ook sprake kan zijn van intact inzicht. Inzicht is een overkoepelende term die verwijst naar het reflecteren op en bewustzijn van functioneren in een bepaald domein, zoals het fysieke, cognitieve of emotionele domein. Inzicht van het cognitieve domein wordt ook wel metacognitie genoemd. In dit proefschrift worden beide termen gebruikt. Verminderd inzicht na NAH is een belangrijk klinisch probleem, maar wetenschappelijk onderbouwde behandelingen ontbreken nog. Dit komt deels doordat onduidelijk is wat inzicht is op conceptueel niveau en hoe verminderd inzicht veroorzaakt wordt. Inzicht is moeilijk te vatten en er bestaan verschillende modellen om het concept te beschrijven. Het is een breed begrip dat allerlei gedragsdomeinen omvat en komt mogelijk tot stand door meerdere onderliggende factoren.

Het doel van dit proefschrift was om een bijdrage te leveren aan het begrijpen, meten en behandelen van verminderd inzicht na NAH. We onderzochten metacognitie bij mensen zonder NAH en onderscheidden de verschillende elementen waaruit het bestaat. Vervolgens werden hersengebieden geïdentificeerd die geassocieerd zijn met metacognitie. In de andere studies in dit proefschrift werd inzicht bij mensen met NAH onderzocht. We bestudeerden op een systematische manier de literatuur om hersengebieden te identificeren die geassocieerd zijn met verminderd inzicht na NAH, we hebben de aard en ernst van verminderd inzicht na traumatisch hersenletsel onderzocht, psychometrische eigenschappen van een instrument om verminderd inzicht te meten beoordeeld, en de effectiviteit van Socratische Feedback therapie geëvalueerd als behandeling om verminderd inzicht na NAH te verbeteren.

In hoofdstuk 2 geven we een overzicht van de verschillende elementen van metacognitie en hoe deze gemeten kunnen worden. Metacognitie bestaat uit twee hoofdelementen: metacognitieve kennis en online inzicht. Online inzicht bestaat ook uit twee elementen: anticipatie van prestatie en het herkennen van fouten. In deze studie hebben we onderzocht in hoeverre deze verschillende elementen met elkaar samenhangen. Er waren 128 gezonde deelnemers die een vragenlijst invulden om metacognitieve kennis te meten en twee cognitieve taken deden waarmee we de verschillende elementen van online inzicht konden meten. We vonden dat de scores op de verschillende elementen van metacognitie normaal verdeeld waren. Dit betekent dat er grote individuele verschillen zijn: de scores varieerden van laag tot hoog, waarbij de meeste mensen ongeveer in het midden scoorden. De offline maten van metacognitie waren niet geassocieerd met de online maten van metacognitie. De offline maten waren echter wel met elkaar geassocieerd, zo waren ook de online maten waren met elkaar geassocieerd. Dit wijst op een duidelijk onderscheid tussen offline en online elementen van metacognitie. Hier moet rekening mee worden gehouden in toekomstig onderzoek en in de kliniek. Inzicht is een breed concept en kan niet worden gemeten met één globaal instrument. In plaats daarvan moeten de afzonderlijke elementen rechtstreeks worden gemeten.

Hoofdstuk 3 beschrijft een studie waarin we de activiteit van bepaalde hersennetwerken onderzochten tijdens een metacognitieve taak. Deze hersennetwerken waren het anterieure en posterieure default mode netwerk en het salience netwerk. Tweeënveertig gezonde deelnemers deden een geheugenherkenningstaak terwijl hun hersenactiviteit werd gemeten in een MRI-scanner. De geheugentaak werd aangepast zodat de deelnemers na elke vraag moesten aangeven hoe zeker deelnemers waren dat hun antwoord correct was. De hersenactivatie tijdens het aangeven van dit vertrouwen in hun antwoord werd geanalyseerd. De vragen waarin het vertrouwen overeenkwam met de nauwkeurigheid van hun antwoord (bijvoorbeeld een hoog vertrouwen voor correcte antwoorden) werd vergeleken met vragen waarin dat niet het geval was (bijvoorbeeld een hoog vertrouwen voor incorrecte antwoorden). Wij vonden aanwijzingen dat de linker midden frontale gyrus, de superieure frontale gyrus, de precuneus en de rechter insula actiever waren tijdens het aangeven hoe zeker ze zijn van hun antwoord wanneer deze overeenkwam met de nauwkeurigheid dan wanneer dit niet het geval was. Vervolgens werd dit verschil in activiteit tussen de twee soorten vragen gecorreleerd met de verschillende elementen van metacognitie. Wij vonden aanwijzingen dat hersenactiviteit in de middelste frontale gyrus geassocieerd was met kennis van cognitie en hersenactiviteit in de insula geassocieerd was met regulatie van cognitie (beide elementen van offline metacognitie). Er waren geen correlaties met een online maat voor metacognitie (AUROC2). Deze bevindingen suggereren dat de verschillende elementen van metacognitie niet alleen te onderscheiden zijn op gedragsniveau (hoofdstuk 2), maar ook op neuraal niveau. Verschillende hersennetwerken lijken betrokken te zijn bij de verschillende aspecten van metacognitie.

Om de neurale correlaten van inzicht na NAH te identificeren, werd een systematisch literatuuronderzoek uitgevoerd die wordt gepresenteerd in hoofdstuk 4. Na uitgebreid de literatuur te doorzoeken werden acht studies over dit onderwerp gevonden. Deze waren moeilijk samen te vatten omdat zij gebruik maakten van verschillende methoden om inzicht te meten die niet direct vergelijkbaar waren. Daarom werden de resultaten van de studies ingedeeld in de verschillende meetmethodes. De resultaten gaven aan dat slecht anticiperen op toekomstige problemen in verband werd gebracht met hersenbeschadiging in de rechter frontale kwab en een verhoogde diffusie in de witte stof van de hersenen. Slechte prestaties op (zelfregulatie)taken waarin metacognitie impliciet werd gemeten door evaluatie van het aanpassen van gedrag, werden geassocieerd met minder functionele connectiviteit van het fronto-pariëtale controlenetwerk naar anterieure cingulate cortex en inferieure frontale gyri. Er was ook meer activatie in de linker insula en het linker pariëtale operculum. Slechtere herkenning van fouten was geassocieerd met minder connectiviteit tussen de default mode netwerk en salience netwerk bij mensen met NAH, terwijl deze associatie juist andersom was in de gezonde controlegroep. Concluderend, na NAH worden verschillen in hersenactivatie en connectiviteit gevonden afhankelijk van het gemeten niveau van inzicht.

De aard en ernst van verminderd inzicht (impaired self-awareness; ISA) en ontkenning (denial of disability; DD) in een groep thuiswonende mensen met traumatisch hersenletsel werd onderzocht in hoofdstuk 5. Hierbij werd gebruik gemaakt van de Clinician's Rating Scale for evaluating Impaired Self-Awareness and Denial of Disability after brain injury (CRS-ISA-DD). Daarnaast werden de psychometrische eigenschappen van het instrument beoordeeld. Slechts 42% van de benaderde personen stemden in met deelname aan dit onderzoek. Dit geeft aan hoe lastig het is om onderwerpen als verminderd inzicht en ontkenning te bestuderen. De meeste deelnemers vertoonden ten minste één symptoom van

ISA en DD, maar de ernst van deze symptomen was laag. De ISA-ernstscores correleerden met neuropsychologische testscores en ernst van het letsel, terwijl DD-ernstscores correleerden met angst. Dit wijst erop dat de twee constructen verschillende onderliggende oorzaken kunnen hebben die verschillende behandelingen vereisen. Psychometrische evaluatie van het instrument toonde aan dat het invullen van de CRS-ISA-DD minder dan 10 minuten duurt en dat het een betrouwbaar en haalbaar instrument is. Wij raden aan om het instrument te gebruiken als diagnostisch instrument om onderscheid te maken tussen ISA en DD wanneer verminderd inzicht na hersenletsel al is vastgesteld.

Een nieuwe behandeling gericht op het verbeteren van verminderd inzicht na NAH werd ontwikkeld en de effectiviteit ervan werd geëvalueerd in hoofdstuk 6. De Socratische Feedback therapie bestaat uit discussie gebaseerd op het Socratisch motiveren, het oefenen van taken en psycho-educatie. Deze therapie was al haalbaar en effectief gebleken in eerdere single-case experimental design studies met vier patiënten. In de huidige grotere multicenter gerandomiseerde gecontroleerde studie met 64 NAH-patiënten die verminderd inzicht hadden, werd de nieuwe interventie vergeleken met standaardzorg. Het doel was om het effect van de therapie te meten op niveau van inzicht, motivatie voor en deelname aan therapie, stemming, kwaliteit van leven en sociale participatie op de lange termijn. De resultaten laten zien dat het inzicht in beide groepen toenam in de loop van de tijd. Alleen tussen 9 en 12 maanden was er een verschil tussen de groepen: het inzicht (gemeten door de PCRS patiënt-naaste verschilscore) verbeterde in de Socratische Feedback groep en verslechterde in de standaardzorg groep. Er werden geen significante verschillen gevonden op de andere uitkomstmaten. Wij concluderen dat Socratische Feedback therapie even effectief is als standaardzorg, maar dat toekomstig onderzoek mogelijk grotere effecten laat zien wanneer medepatiënten en naasten nauw betrokken worden bij de cognitieve therapie. De Socratische Feedback therapie kan worden beschouwd als alternatief voor standaardzorg omdat het protocol structuur en handvatten biedt voor therapeuten die patiënten met een verminderd inzicht na NAH behandelen.

Hoofdstuk 7 bevat de algemene discussie van dit proefschrift. De belangrijkste bevindingen worden geïntegreerd en methodologische overwegingen worden besproken. Daarnaast worden implicaties voor de kliniek en toekomstig onderzoek beschreven. De bevindingen in dit proefschrift laten zien dat metacognitie uit verschillende elementen bestaat die van elkaar te onderscheiden zijn. Deze elementen kunnen worden gemeten met verschillende meetmethoden en lijken gerelateerd aan verschillende hersennetwerken. Verminderd inzicht kan via verschillende wegen ontstaan. Het kan bijvoorbeeld een neurocognitieve of psychologische oorsprong hebben. De oorsprong kan worden vastgesteld met behulp van de Clinician's Rating Scale for evaluating Impaired Self-Awareness and Denial of Disability (CRS-ISA-DD), die kan worden gebruikt om te helpen bepalen welke behandeling moet worden geïndiceerd. De Socratische Feedback therapie is een alternatief voor standaardzorg. Deze behandeling is even effectief wat betreft het vergroten van het inzicht na NAH, en eventuele bijkomende effecten zijn mogelijk nog verborgen. In het algemeen is duidelijk geworden dat het belangrijk is specifiek te zijn in welk element van inzicht iemand in geïnteresseerd is, dat element goed te meten, en de behandeling daarop af te stemmen. Wij geven handvatten hoe dit op een gestructureerde manier verder onderzocht kan worden. Een belangrijke les die we geleerd hebben is dat we het bestuderen van inzicht moeten benaderen als het eten van een olifant: hap voor hap.

IMPACT PARAGRAPH

Impact paragraph

Impact paragraph

The studies in this thesis concern a problem that is encountered in clinical practice during rehabilitation after acquired brain injury (ABI). Namely, after sustaining an ABI, it is common for people to have impairments in a variety of cognitive functions, such as memory, attention, or decision-making. However, some people have difficulties recognizing that, or how, their behavior has changed due to the ABI. This is called impaired self-awareness and can hinder rehabilitation. People with impaired self-awareness might not understand or see the need for treatment and are less motivated to participate in treatment. This can cause frustration for the patient, who does not understand why they should change, but also for the therapists and significant others, who want to help but feel they are not being heard. This can lead to conflict between these parties. The aim of this thesis was to investigate what self-awareness is conceptually, what the underlying causes of impaired self-awareness are, and how it can be treated.

Main findings

The studies described in this thesis, combining studies in patients and healthy subjects, confirm that self-awareness of cognitive functioning, also known as metacognition, consists of different distinguishable elements which makes it hard to grasp as a whole. The elements can be measured in different ways. For example, questionnaires can be used to get a more general overview of someone's beliefs about their cognition, while confidence judgments related to one's specific answers on a cognitive task measure a more specific and dynamic element of metacognition. The studies in this thesis also indicate that there are different brain networks that are involved in the different elements of metacognition and that brain injuries in these different networks are associated with impairments in different elements of self-awareness. After ABI, impaired self-awareness can arise in several ways. Damage to the brain can disrupt brain networks that are necessary for self-awareness, but impaired self-awareness can also arise through a coping mechanism associated with the traumatic event of having an ABI, such as denial. In our studies we found evidence for this distinction. Namely, performance on cognitive tasks and injury-related factors, such as severity of the injury, were associated with neurocognitive impaired self-awareness, while denial of disability was associated with anxiety. A new intervention, Socratic Guided Feedback therapy, was investigated as a possible treatment for impaired self-awareness and compared to care as usual. We found that the new treatment was just as effective as the standard practices in rehabilitation centers. Through these studies, we have gained a lot of information on how future research and treatments should be set up and conducted.

Scientific impact

The studies in this thesis have been published, or have been submitted to be published, in open access international peer-reviewed journals. Results have also been presented at national and international conferences. Our findings contribute to scientific research by adding knowledge on theoretical models and treatment of self-awareness. This thesis provides a thorough investigation of self-awareness with a focus on self-awareness of cognition. Having investigated this in people with and without ABI, our findings can help scientists understand metacognition and how impairments can occur after ABI. This thesis provides a theoretical overview of the different elements metacognition consists of and how these can be measured. We emphasize the need to be specific when studying this topic. This implies that scientists should be clear on which element of metacognition they are studying. This can help us compare studies and understand metacognition even better. With the studies in this thesis we provide tools on how metacognition can be further investigated in a structured way. For example, the imaging study in chapter 2 has proven to be a feasible set-up in healthy people that can now be used in people with ABI to investigate neural correlates of metacognition in that population. This is not only relevant for scientists in the ABI rehabilitation field but could also be translated to studies concerning metacognition in any other population or field, such as in patients with dementia, or in the field of educational psychology.

Societal impact

People with ABI as well as clinicians and therapists working in rehabilitation centers were directly involved in some of the studies in this thesis. Therefore, the findings in this thesis have direct implications for anyone involved in health care practice and, more specifically, neuropsychological rehabilitation after ABI. Firstly, through creating better theoretical foundations of self-awareness and how this can be impaired, we offer better understanding for therapists, patients, as well as significant others and caregivers. This could clarify some of the questions these individuals might have, which could already relieve some burden for them. Secondly, the Socratic Guided Feedback protocol can help therapists feel more secure when treating a patient with impaired self-awareness which can, in turn, improve the outcomes of the therapy. In a similar way it can offer significant others and caregivers grip on how to communicate with their loved ones. At the same time, Socratic Guided Feedback therapy can help patients feel more understood. Taken together, this can decrease friction and conflict, relieve burden, and improve quality of life for everyone involved. Additionally, this thesis has implications for students in the neuropsychological field. Through lectures and tutorials they can learn about theoretical and neurobehavioral factors related to self-awareness.

Dissemination activities

The findings in this thesis have been disseminated in different ways. They have been shared with the scientific community through publication in open access international peer-reviewed journals and are accessible to read for scientists or anyone interested. The papers that are not published yet have been submitted for publication in such journals. Moreover, the datasets are, or will be, accessible on request for use in future research. The results have been presented at international conferences such as the International Neuropsychological Society (INS), Special Interest Group of the World Federation for NeuroRehabilitation (NR-SIG-WFNR), and International Brain Injury Association (IBIA). Additionally, the findings have been shared with the professional community through symposia and webinars organized by the Brain Injury Center Limburg. We have shared the findings in this thesis with the general public too. This was achieved through presentations at informal public meetings organized for people with ABI and their partners such as Brain Cafes. The findings have also been spread in a podcast episode of the Stroke Knowledge Network in the Netherlands. For the chapters that remain to be published, we will share the findings with the participants through newsletters. Finally, we have updated the general public about the findings through social media such as our website www.hersenletsellimburg.nl, LinkedIn, and Twitter.

CURRICULUM VITAE

Curriculum vitae

About the author

Anneke Terneusen was born in Fijnaart en Heijningen on January 26th, 1995. She completed her secondary education (bilingual VWO) at Elde College in Schijndel. In 2013, she moved to Amsterdam to study Psychobiology at the University of Amsterdam. During her Bachelor's education she studied abroad in Melbourne, Australia for six months after which she completed a research internship at Radboud University Nijmegen. Here she conducted research and wrote her Bachelor thesis on the effects of a medication (Befiradol) on aggression. In 2016, Anneke moved to Maastricht to obtain her Research Master's degree in Cognitive and Clinical Neuroscience, with a specialization in Neuropsychology at Maastricht University. Her research internship and Master thesis concerned the relation between self-awareness of deficits, motivation for therapy, and participation in therapy during acquired brain injury rehabilitation. In 2018, Anneke became part of Brain Injury Centre Limburg and started her PhD project at the Faculty of Psychology and Neuroscience at Maastricht University. She investigated impaired self-awareness after acquired brain injury under supervision of Prof. Dr. Caroline van Heugten, Prof. Dr. Rudolf Ponds, and Dr. Ieke Winkens. During this PhD trajectory she was also involved in education at Maastricht University and obtained her University Teaching Qualification. Anneke currently works as research coordinator at the Faculty of Health, Medicine and Life Sciences at Maastricht University where she continues her career conducting research on Parkinson's disease.

Publications and presentations

Publications

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