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Understanding Self-Awareness in Activities of Daily Living:

Alterations After Brain Injury, Cognitive Components and Neural Bases

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Esta es la parte más difícil de escribir, y esto, después de todo lo que ha venido antes lo dice todo. Es prácticamente imposible expresar en pocas líneas todo lo que siento para todas las personas que han estado conmigo en los últimos cinco años. Pero es también imprescindible para poner la guinda a este trabajo, porque sin la presencia de todas estas personas este trabajo no habría sido lo que es.

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ABSTRACTS

Abstract

Self-awareness (SA), understood as the self-perception and belief about our abilities and difficulties, plays a paramount role in performing our activities of daily living (ADL). After suffering an acquired brain injury (ABI), SA can be impaired, which has a dramatic effect on patient functionality. According to main models (*e.g. the Dynamic Comprehensive Model of Awareness; DCMA*) SA is described as being composed of various interacting components. The *offline SA* is the conscious knowledge that we have about our own abilities and/or deficits when dealing with activities that we usually perform. In contrast, *online SA* is composed of several subprocesses that allow us to anticipate, detect and solve problems or errors during task performance. Self-awareness seems not to be an all-or-nothing phenomenon, but it is proposed to be domain-specific and to be highly dependent on prior experience and familiarity with tasks.

The multicomponential and task-dependent nature of SA entails the need to develop new comprehensive SA evaluation tools that include the measurement of both offline and online components of SA, all within the context of the same functional domain. This would help to identify the specific SA component that may be impaired in any given ABI patient. Furthermore, research is still necessary to better understand the specific cognitive and neural components involved in online SA,

In the present thesis we aimed to address all these aspects of SA within the context of ADL. We believe that ADL provide an optimal setting for studying SA due to their familiarity and the diversity of behaviors observed during their performance, enhancing the ecological validity of the research.

In Study I (Ricchetti et al., in press) we tested the validity of the Breakfast and Dressing Conflict Task, a comprehensive assessment protocol previously proposed in our lab (Merchán-Baeza et al., 2020) with the potential to evaluate the main components of online SA in the context of familiar ADL in ABI patients and healthy participants. The ADL-based measures of online SA derived from the proposed protocol showed convergent validity with traditional neuropsychological measures. Some of the ADL-based measures successfully identified online SA impairments in ABI patients when compared to healthy controls. Furthermore, the associations found between some of the ADL-based online SA measures and the offline component of SA supported the interactional nature of SA proposed by the DCMA.

In Study II we deepened on the study of the specific cognitive components of SA, with a particular focus on the potential relationship between SA and executive function (EF). The contradictions found in previous research (with some study supporting and other rejecting such association), may be related to the multicomponential nature of both constructs. Therefore, we hypotesize that specific components of SA may be associated with specific components of EF. To explore this hypothesis, in Study II we investigated the relationship between conflict monitoring/resolution (a specific component of EF) and offline SA and emergent awareness (*i.e.* error detection). We studied this potential relationship by combining the use of a conflict-based experimental task with an ADL-based questionnaire and an ADL performance-based task in ABI patients and healthy controls. We found that ABI patients with severly impaired SA showed reduced conflict monitoring/resolution abilities compared to ABI patients with no/low SA impairments and compared to healthy controls. In addition the ability to monitor and solve conflicts during the experimental task predicted the rate of errors detected during the perofrmance-based ADL task as well as the level of offline ISA measured with the ADL-based questionnaire.

Finally, in Study III we investigated the neural bases of error detection in healthy participants. Previous research revealed both shared and different neural networks in relation to different types of errors in both experimental and ADL-based error research. In Study III we further investigate this qualitative differentiation, focusing on the errors that occur due to the alteration of the correct sequence of steps in ADL (*e.g.* omissions, repetitions or order violations of steps). The results of this study revealed that different neural networks are involved in the detection of the different types of sequence errors. In addition, the study of the sequential aspect also allowed us to identify the involvement of different neural networks in the monitoring of ADL sequence steps depending on their predictability.

The results of the present thesis contribute to enhancing our understanding of how SA works and of the potential factors that are involved in its alterations after an ABI, with significant implication for clinical practice. Furthermore, the findings presented in this dissertation suggest some important factors that may be taken into account when studying SA and its alterations. Firstly, it is important to consider the multicomponential and domain-specific nature of SA and to use measures that permit studying the different components of SA in a specific and ecological manner. Secondly, study II highlights the enriching potential of studying SA combining different methodologies. Finally, this thesis sheds light on the need to apply a qualitative approach to studying SA, which allows for a deeper understanding of its cognitive and neural components and may be helpful to identifying various patterns and profiles of SA alteration.

Resumen

La autoconsciencia (AC), entendida como la percepción y creencias que tenemos sobre nuestras habilidades y limitaciones, juega un papel importante en el desempeño de nuestras actividades de la vida diaria (AVD). Después de un daño cerebral adquirido (DCA), los déficits de AC tienen efectos dramáticos en la funcionalidad de los pacientes. Según los principales modelos (*e.g. the Dynamic Comprehensive Model of Awareness; DCMA*) la AC está compuesta por varios componentes que interactúan entre sí. La AC *offline* es el conocimiento consciente que tenemos sobre nuestras habilidades/limitaciones para enfrentar nuestras AVD. Por otro lado, la AC *online* está compuesta por varios subprocesos que nos permiten anticipar, detectar y solucionar problemas durante el desempeño de una actividad específica. La AC no es un fenómeno de todo o nada, sino que parece ser específica para cada dominio y parece depender en gran medida de las experiencias previas y de la familiaridad con las tareas.

La naturaleza multicomponente y tarea-dependiente de la AC, conlleva la necesidad de desarrollar nuevos instrumentos de evaluación que permitan evaluar de forma exhaustiva tanto el componentes offline como los procesos online del a AC, todos en el contexto del mismo dominio funcional. Esto permitiría identificar qué componentes de la AC están alterados en cada paciente con DCA. Además, resulta necesaria más investigación para entender mejor cuáles son los componentes cognitivos y neurales involucrados en la AC online.

El objetivo de la presente tesis es abordar cada uno de estos aspectos de la AC en el contexto de las AVD. Creemos que las AVD representan el contexto ideal para estudiar la AC, debido a su familiaridad y a la diversidad de comportamientos que se pueden

observar durante su desempeño, lo que a su vez incrementará la validez ecológica de la investigación.

En el estudio I (Ricchetti et al., aceptado) testamos la validez de la "Tarea Conflictiva del Desayuno y Vestido", un protocolo de evaluación propuesto por nuestro laboratorio (Merchán-Baeza et al., 2020) que tiene el potencial de evaluar los principales componentes de la AC online en el contexto de AVD en pacientes con DCA y en personas neurológicamente sanas. Las medidas de AC online derivadas del protocolo de AVD mostraron validez convergente con medidas neuropsicológicas tradicionales. Algunas de las medidas de AVD permitieron identificar alteraciones de AC online en pacientes con DCA, en comparación con controles sanos. Además, las asociaciones encontradas entre algunos componentes de la AC online y el componente offline apoyan la naturaleza interactiva de la AC propuesta por el DCMA.

En el estudio II profundizamos en el estudio de los componentes cognitivos específicos de la AC, con particular atención a la relación entre la AC y las funciones ejecutivas (FFEE). La falta de resultados consistentes en la literatura, donde algunos estudios confirmaron y otros descartaron esta asociación, puede ser debida a la naturaleza multi-componente de ambos constructos. Así, creemos que componentes específicos de la AC pueden estar asociados a componentes específicos de las FFEE. Para explorar esta hipótesis, en el estudio II investigamos la posible relación de la monitorización/resolución de conflictos (componente específico de las FFEE) con la AC offline y con la consciencia emergente (*i.e.* detección de errores). Esta relación se ha estudiado combinando el uso de tareas experimentales de conflicto con cuestionarios y desempeño directo de AVD en pacientes con DCA y controles sanos. Encontramos que los pacientes con DCA y alteración severa de la AC mostraron una reducida capacidad de monitorizar y solucionar los conflictos en comparación con pacientes con DCA sin alteración de AC (o con alteración leve) y con controles sanos. Además, encontramos que la habilidad de monitorizar y solucionar los conflictos durante la tarea experimental podía predecir la cantidad de errores durante el desempeño de tareas cotidianas y el nivel de consciencia medido con cuestionarios basados en AVD.

Finalmente, en el estudio III investigamos las bases neurales de la detección de errores en participantes sanos. La investigación previa ha encontrado circuitos cerebrales compartidos pero también diferentes en relación a la detección de diferentes tipos de error, tanto en tareas experimentales como en tareas de AVD.

En el estudio III investigamos estas diferencias cualitativas, focalizándonos en los errores causados por la alteración de la secuencia correcta de pasos en las AVD (*i.e.* omisión, repetición e inversión de pasos). Los resultados de este estudio mostraron que diferentes circuitos cerebrales están involucrados en la detección de los diferentes tipos de errores de secuencia. Además, el estudio del aspecto secuencial de los pasos de las AVD permitió identificar que diferentes circuitos cerebrales se encargan de monitorizar las acciones de las AVD dependiendo de su predictibilidad.

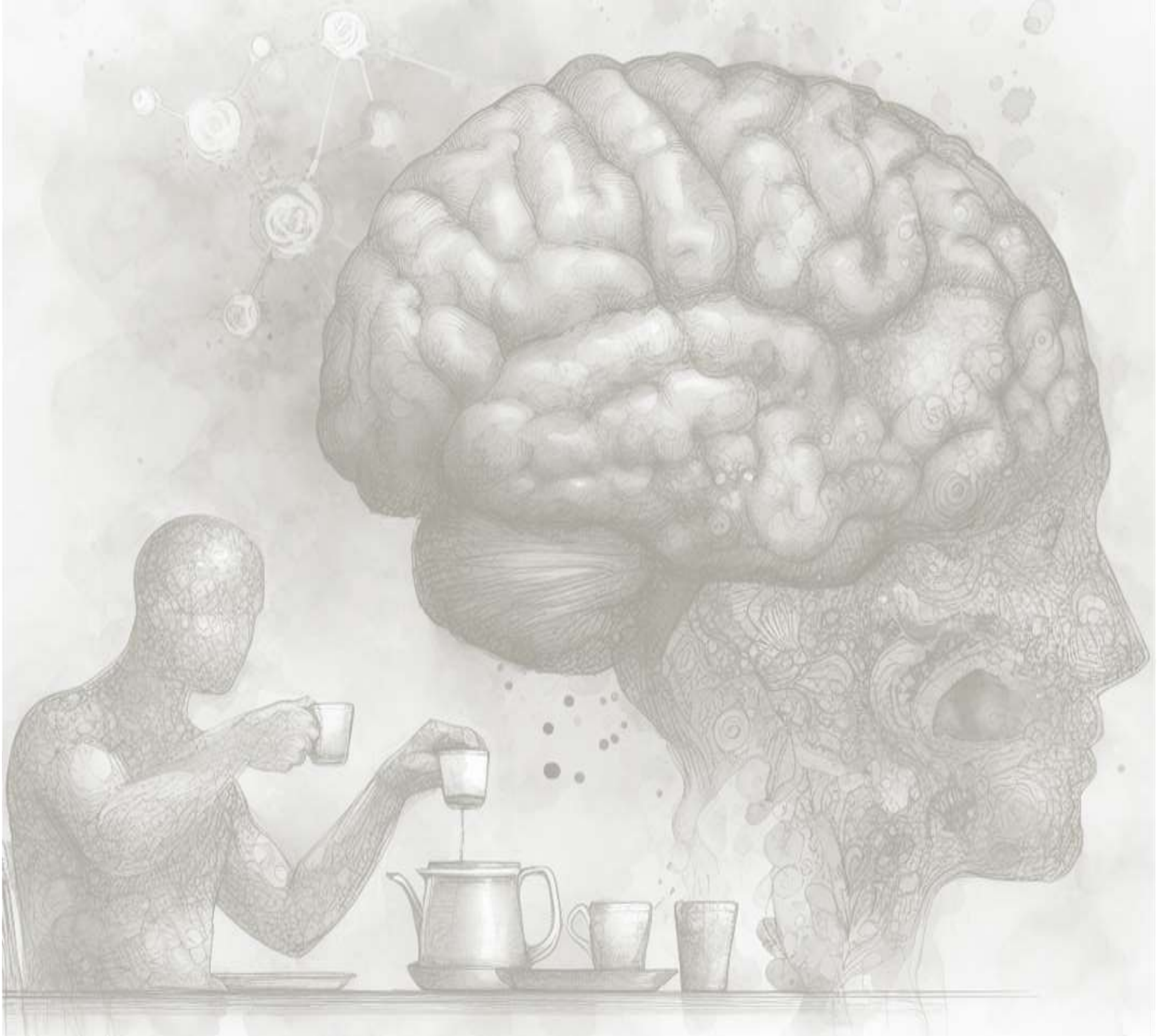
Los resultados de la presente tesis contribuyen a aumentar nuestro conocimiento sobre cómo funciona la AC y sobre los factores que pueden estar involucrados en su alteración tras un DCA, con implicaciones significativas para la práctica clínica.

Además, los hallazgos de esta tesis sugieren algunos aspectos importantes a tener en consideración en el estudio de la conscienica y sus alteraciones. En primer lugar, es importante considerar la naturaleza multicomponente y dependiente del dominio de la AC y utilizar medidas que permiten estudiar los diferentes componentes de la AC de forma específica y ecológica. En segundo lugar, el estudio II resalta el potencial enriquecedor que tiene combinar diferentes metodologías para el estudio de la consciencia.

Finalmente, esta tesis pone en evidencia la necesidad de aplicar un abordaje cualitativo a la hora de estudiar la AC, lo cual permitiría comprender de manera más eshaustiva sus componentes cognitivos y neurales y podría ayudar a identificar diferentes patrones y perfiles de alteración de AC.

PART I

INTRODUCTION



CHAPTER 1

Understanding Self-Awareness and its Alterations

1.1 What is anosognosia?

The understanding of human consciousness has been the focus of study of very different disciplines such as philosophy, neurology and psychology (Galin, 1992). The study of consciousness as a neurological and neuropsychological phenomenon started with the observation of a particular condition where patients with neurological lesions seemed not to be aware of their neurological symptoms. First forms of unawareness of deficits were described in patients with cortical blindness and deafness by Anton in 1899. However, it was not until the year 1914 that Babinski coined the term *anosognosia* (composed of the three Greek terms *nosos* meaning disease, *gnosis* meaning knowledge and the privative prefix *a)* to refer to this neurological unawareness of deficits (Prigatano & Schacter, 1991). Babinski first used the term anosognosia to describe the patients' lack of acknowledge of their hemiplegia after an acquired brain injury (Gainotti, 2018; Prigatano, 2014). When asked by the clinician about their paralyzed arm, these patients did not report any issues related to their limb; instead, they indicated that their arm was fine. After that the term anosognosia has been extended beyond unawareness of hemiplegia and used to describe lack of awareness of any possible symptoms derived from a neurological dysfunction, including physical, cognitive and socio-emotional deficits (Dromer et al., 2021a; Gasquoine, 2016; Prigatano, 2014). Besides the term anosognosia, several other terms are used to refer to this particular condition such as reduced self-awareness, impaired self-awareness (ISA), unawareness of deficits and lack of awareness (Galin, 1992; Gasquoine, 2016; Marková & Berrios, 2006; Prigatano & Schacter, 1991) These terms are used indistinctly throughout the present thesis with the purpose of referring to the condition in which the patient under-reports or underestimates their functional symptoms.

Anosognosia is not an all or nothing phenomenon and it has been documented that patients may present different levels of self-awareness about different domains (Prigatano, 1996, 2012, 2014). Several studies have described that patients usually have more awareness of more visible deficits (*e.g.* physical deficits) while unawareness of deficits is greater for abstract domains, such as cognitive and emotional domains (Chesnel et al., 2017; Dromer et al., 2021b; Malouf et al., 2014; Prigatano et al., 1990; Sherer et al., 2003). In the present thesis we are focusing on anosognosia about cognitive deficits. Anosognosia can also be classified in relation to its severity as mild, moderate or severe ISA (Prigatano, 2010). Although mild forms of ISA may have little impact on patients' everyday life, severe ISA represents a complication with major consequences for the patient's functionality and independence (Sherer et al., 2003). First of all, patients with severe anosognosia usually perform activities that exceed their abilities and can't adapt their daily performance to the cognitive deficit, giving rise to dangerous situations (Crosson et al., 1989; Fischer et al., 2004; Fleming & Strong, 1999; Hartman-Maeir et al., 2001, 2003). As an example, let's imagine a patient with memory impairments who decides to cook a pie in the oven. If the patient is completely aware of their memory impairment, they will probably use an alarm to make sure they take the pie out of the oven. However, a patient lacking awareness of their memory deficits might fail to use this adaptation since they believe that they will be able to remember. Clearly this could result in burning the pie or even worse. In addition, these behaviours might be maintained over time, since severe anosognosia is also a major obstacle for patient's recovery. Patients with unawareness of cognitive deficits don't engage in the rehabilitation process, considering it unnecessary (Fischer et al., 2004; Fleming & Strong, 1999; Hartman-Maeir et al., 2001, 2003). Going back to the example of the patient with anosognosia about their memory impairment, why should they attend rehabilitation sessions and make activities to improve their memory, if they don't have any memory impairments? All these complications result in high dependence and caregiver burnout (Fischer et al., 2004; Hartman-Maeir et al., 2001, 2003b).

1.2 Theoretical models and components of anosognosia

Anosognosia is a complex construct and this complexity is clearly reflected in the theoretical models developed to explain and understand it. All these models, mainly developed within the Neuropsychology and Occupational Therapy fields, describe SA as a multicomponent construct. The first model of self-awareness in acquired brain injury was proposed by Crosson et al. in 1989. The authors describe self-awareness as a pyramid composed of three types of awareness. The *intellectual awareness* is at the lowest level of the pyramid and relies on the understanding that a particular deficit is present (*e.g.* my memory is impaired) and the consequences of these deficits (*e.g.* I can't remember my work appointments). The second level of the awareness pyramid is composed of *emergent awareness*, which is the ability to recognize problems in the moment they occur. Finally at the top level of the pyramid there is the *anticipatory awareness* that is the ability to anticipate that a problem will occur as the result of the deficit. In this model the three levels are interdependent with the lower level being a prerequisite for the next one. Rare are the cases where the bottom level is intact and the top is impaired (Crosson et al., 1989).

After this, other models have been developed, all proposing a multicomponential structure (Agnew & Morris, 2010; Clare, 2004; Prigatano & Schacter, 1991; Schacter, 1990; Toglia & Kirk, 2000). The Dynamic Comprehensive Model of Awareness (DCMA, Toglia & Kirk 2000) is one of the most influential models and constitutes the framework of the present thesis. Similarly to Crosson et al.'s model this model defines different components of self-awareness. The *metacognitive knowledge* is the *offline* component of self-awareness since it exists prior to task performance (corresponding to the intellectual awareness in the Crosson et al.'s model; 1989). This offline component consists of generic semantic knowledge, stored in long-term memory, about tasks characteristics and self-knowledge about our abilities/difficulties. For example, this component contains knowledge such as "I am a good dancer" or "I'm not good at cooking". However, a comprehensive metacognitive knowledge needs general semantic knowledge about the characteristics of the tasks and also contains information such as "Cooking a *paella* is more difficult than making a sandwich". Based on this knowledge, I know that I might have more or less difficulties in performing a [cooking] task depending on its characteristics (*e.g.* difficulty, familiarity, significance).

A second component of self-awareness is the *online* one, which is activated within the performance of a specific task. The online component of self-awareness is composed of subcomponents such as *anticipatory awareness*, *emergent awareness, self-regulation and self-evaluation*. Anticipatory awareness is the ability to predict situational demands and likely problems during the performance of the specific incoming task. Emergent awareness (*i.e.* performance monitoring and error detection) and self-regulation (*i.e.* performance adaptation and error correction) are the processes that permit a moment-by-moment awareness of the performance and the adaptation of performance as needed.

Immediately after the completion of the task the self-evaluation begins, comparing the current performance with the expected performance (Toglia & Kirk, 2000).

Meanwhile Crosson et al.'s (1989) model considers the different awareness components as interdependent in a hierarchical manner, an important aspect of the DCMA is, exactly as its name suggests, that the interaction among the different components and subcomponents of self-awareness is dynamic in nature (Toglia & Goverover, 2022; Toglia & Kirk, 2000). Consequently, the information about ourselves and about tasks characteristics contained in the metacognitive knowledge is necessary in order to understand and anticipate the difficulties that we could face while performing a specific approaching task, thus enabling appropriate anticipatory awareness. For example, following with the cooking example, I might anticipate that I would have some difficulty preparing a *paella* but I don't anticipate any problem when I am approaching making a sandwich. Anticipatory awareness, in turn, affects the amount of cognitive resources applied during the task, including performance monitoring resources that might influence emergent awareness ability. During the performance of the task, a proper emergent awareness (*i.e.* difficulty and error recognition) enables a self-regulation process during the task performance and a proper self-evaluation afterwards. Finally, a correct self-evaluation of our recent performance and the integration of this information in our long term-memory are important in order to *update* our previous metacognitive knowledge, especially when a discrepancy between the expected (or anticipated) performance and actual performance is found. The way I'm going to face the same activity in the future depends on this process (Toglia & Kirk, 2000). Figure 1.1 depict a graphical representation of the DCMA and its dinamic interactions.

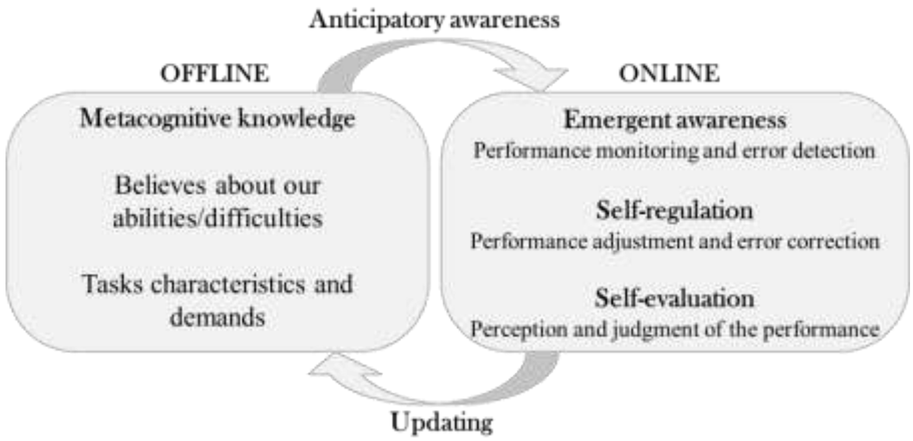


Figure 1.1 Representation of the components and subcomponents of the Dynamic Comprehensive Model of Awareness and their interaction (adapted from Toglia & Kirk, 2000)

Based on the DCMA, one straightforward assumption is that different forms of anosognosia could arise depending on the affected component or process. Upholding this idea, different profiles of patients with unawareness of deficits have been described in the literature. On the one hand the so-called executive anosognosia is caused by an impairment of the online performance monitoring system (Mograbi et al., 2009; O'Keeffe et al., 2007; Toglia & Kirk, 2000). In this case, a lack of error signaling during task performance hinders the patient from recognizing problems when they occur, and therefore, this information cannot be integrated in patient's self-knowledge. A second form of anosognosia, more related to memory consolidation impairments, has been widely described in the context of neurodegenerative disease, in particular in Alzheimer's disease. In this case, if the monitoring system is not largely affected the patient may be able to detect their problems during task performance. However, due to memory deficits, this information might vanish with the passing of time and as a result, it will not be integrated in the metacognitive knowledge either. This is a type of ISA typically known as "petrified self" (Agnew & Morris, 2010; Crosson et al., 1989; Mograbi et al., 2009; Toglia & Goverover, 2022). Some patients may exhibit specific self-regulation problems and struggle to efficiently correct errors when detected. Additionally, selective impairments in self-evaluation have been described, with preserved error detection and correction (Morris & Mograbi, 2013; Scherling et al., 2017; Toglia & Kirk, 2000). In these cases, the patient may successfully detect and correct errors, but the issue lies in their perception and judgment of the importance of events such as errors on their overall performance.

The impairment described above, each reflecting the alteration of a different component of SA, lead to the same consequence in offline SA, with the patient showing an unreal belief about their abilities and difficulties. This highlights the importance of isolating and focusing on the specific component/s and processes that are contributing to unawareness in a given patient, in order to implement the most adequate treatment for them (Fleming & Ownsworth, 2006).

CHAPTER 2

Cognitive Components of Self-Awareness

2.1. Self-Awareness and Memory processes

In line with the multicomponential nature of self-awareness proposed by most theoretical models, there is not a unique neuropsychological profile of anosognosia and, as highlighted above, different forms of ISA might be found depending on the cognitive process that are mostly affected (Hannesdottir & Morris, 2007; Ownsworth et al., 2002; Prigatano, 2014). In this section we will review and go deeper on the specific cognitive processes that might underlie SA components.

One of the key cognitive processes that have been proposed to significantly affect anosognosia is memory. This idea was already present in the first SA models (Crosson et al., 1989; Toglia & Kirk, 2000). Crosson et al. (1989) suggested that one of the causes of impaired intellectual awareness (*i.e.* offline SA) was that the patient could not remember their past experience, which constitutes the bases upon self-knowledge is built. Toglia & Kirk (2000) described the integration of the new experiences with the past ones as one necessary mechanism to maintain a proper SA. This idea was further elaborated in the Cognitive Awareness Model (CAM). In this model of anosognosia, proposed by Morris & Hannesdottir (2004) in the context of Alzheimer's Disease (AD), the authors introduced the concept of mnemonic anosognosia (Morris & Hannesdottir, 2004). Mnemonic anosognosia is characterized by the lack of updating of the information about the self in the metacognitive knowledge, referred to as Personal Database in the CAM (Mograbi et al., 2009; Morris & Hannesdottir, 2004; Morris & Mograbi, 2013). This type of ISA seems to be the principal form of anosognosia in AD and neurodegenerative pathologies characterized by episodic autobiographical memory impairments (Lenzoni et al., 2020; Mograbi et al., 2009). The autobiographical memory impairment in AD shows a temporal gradient, with memory for remote experiences remaining relatively preserved and memory for more recent events being specifically impaired (Mograbi et al., 2009). As a result, the patient's self-knowledge remains stable over time and does not adapt to recent personal changes that may arise due to the illness, leading to the condition known as "petrified self" (Lenzoni et al., 2020; Mograbi et al., 2009). As an example, in a single case study Klein et al. (2003) asked K.R. (a patient with AD) and her daughter to rate K.R.'s personality traits. The authors note that the two ratings significantly differed from one another. However K.R.'s self-rating matched with the rating that her daughter had made when thinking of her mother's personality traits prior to her illness. The personality traits of K.R. had changed because of the AD but her self-knowledge had not (Klein et al., 2003). In line with the idea that episodic memory deficits might impact on patients' self-knowledge, several studies found an association between the performance in episodic memory neuropsychological tests and measures of offline ISA in both patients with neurodegenerative disease (Stepanie Cosentino et al., 2007; Gagliardi & Vannini, 2022) and ABI patients (Gilleen et al., 2014; Noé et al., 2005; Villalobos et al., 2021; Zimmermann et al., 2017).

The specific mechanism affecting the updating process in mnemonic anosognosia is an anterograde memory impairment that lead to the impossibility of encoding new events and generating new memories (Lenzoni et al., 2020; Mograbi et al., 2009). Therefore, in this type of ISA, even if online SA (*i.e.* emergent awareness) is not largely impaired and the patient is able to recognize their failure while performing the task, that information vanishes over time and cannot be integrated with the patient's prior metacognitive knowledge. Some studies have directly tested this hypothesis. For example, in Ansell &

Bucks (2006) a sample of AD patients performed three consecutive memory recognition tests. Before each performance the patients were asked to estimate their performance accuracy and in addition, to assess the updating component. After 20 minutes the patients were asked to anticipate the performance in a similar task. The patients showed a significant increase in accuracy prediction from the first to the third test performance, indicating an improvement in anticipatory awareness after the exposure to the task. However, the difference between the delayed prediction and the first prediction was only marginally significant, indicating that after 20 minutes the estimation accuracy had declined (even if it did not reach the pre-test level). Stewart et al. (2010) carried out a similar study where a sample of AD patients had to predict their accuracy on a memory test and rate their performance post-test. In addition, after a 1-hour delay the patients were asked to predict their performance on a similar memory test. Interestingly, the authors found that, similarly to the previous study, patients' self-rating after the performance were significantly more accurate than patients' predictions of performance. However, in this case, the patients' performance predictions after the one-hour delay were significantly less accurate than the immediate post-test self-evaluations. These studies reflect how, as the time goes by, there is a dissipation of the information about the new experiences and this may be one of the key mechanisms underlying ISA in some neuropsychological patients.

2.2. Self-awareness and executive functions

Another cognitive domain highly related to ISA, and more largely studied in patients with ABI, is *executive functions* (EF), with this relationship being evident from multiple perspectives. Based on most self-awareness models, emergent awareness and self-regulation online components resemble the monitoring and regulation processes typically included as core components of EF (Arnould et al., 2016; Kennedy & Coelho, 2005; Miyake et al., 2000; Stuss, 1991). In addition, the concept of *metacognition* may help to better understand the link between self-awareness and EF. Self-awareness models are based and share their structure with models of metacognition (the knowledge about one's own cognitive processes), firstly developed in metamemory research. The first model of metacognition was developed by Nelson & Narens (1990). Two main characteristics are representative of this model: 1) the presence of two interrelated levels, the meta-level and the object-level and 2) the flow of information between the two levels throughout the processes of control and monitoring. The meta-level, constitutes the offline component and the object-level (or experience level) corresponds to the online metacognitive process. Throughout a monitoring process the meta-level receives information from the object-level about the ongoing cognitive functioning. In turn the meta-level gives feedback to the object-level in order to control and regulate the cognitive processes (see Figure 2.1). This control is especially important when the monitoring process informs of a conflict in the object-level that requires behavior adaptation and change of strategy to achieve the main goal.

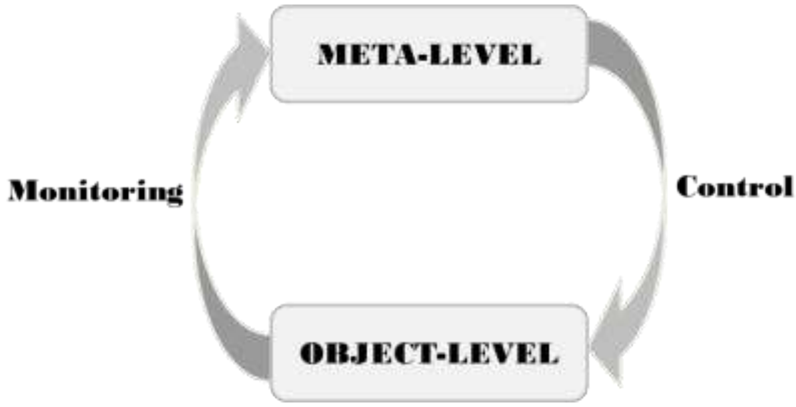


Figure 2.1 Representation of the Model of Metacognition (adapted from Nelson & Narens, 1990)

When thinking of metacognition in these terms, the parallelism with executive functions is evident (Fernandez-Duque et al., 2000; Roebers, 2017). Executive functions are the processes that permit continuous evaluation and regulation of information processing in goal-directed behavior (Cristofori et al., 2019). In addition, as occurrs with metacognition, executive control is fundamental in the presence of conflicting situations that require top-down control to flexibly adapt behavior to the environment, to selectively process relevant-task information and to avoid actions being guided by external irrelevant stimuli. (Fernandez-Duque et al., 2000; Posner & Rothbart, 1998; Roebers, 2017; Shimamura, 2000b, 2013). Probably because of this theoretical parallelism, deficits in EF are among the cognitive domains most studied in relation to ISA (Belchev et al., 2017; Bivona et al., 2019; Bivona et al., 2008; Bogod et al., 2003; Caldwell et al., 2014; Chen & Goverover, 2021; Chiou et al., 2011; Chudoba &

Schmitter-Edgecombe, 2020; Ciurli et al., 2010; Giovannetti, Libon, & Hart, 2002; Goverover, 2004; Hart et al., 2005; Kashiwa et al., 2005; Morton & Barker, 2010; Noé et al., 2005; Trudel et al., 1998; Villalobos et al., 2021; Wise et al., 2005).

The link between ISA and deficits in EF is also evident clinically, as patients with ISA often show dysexecutive behaviors as well (Crosson et al., 1989; Prigatano, 2014; Toglia & Kirk, 2000). Such a relationship has also been confirmed in empirical research. Several studies have reported that executive deficits significantly correlate and even predict deficits in offline and/or online components of self-awareness in patients with neurologic impairments (Bettcher et al., 2008; Bivona et al., 2008; Bogod et al., 2003; Chen & Goverover, 2021; Coben et al., 1995; Hart et al., 2005; Kashiwa et al., 2005; Noé et al., 2005; Villalobos et al., 2021). A similar relationship between SA and EF has also been found in healthy participants (Arora et al., 2021; Zlotnik & Toglia, 2018).

However, not all studies have found a relationship between EF and self-awareness (Bach & David, 2006; Belchev et al., 2017; Chiou et al., 2011; Giovannetti, Libon, & Hart, 2002). One of the reasons for these contrasting findings may be related to the fact that these studies differed on the type of measures of SA and of EF that they used to study the relationship between the two constructs. For example, several studies found a relationship between the rate of perseverative errors from the Wisconsin Card Sorting Test and offline SA when measured with self-informant discrepancy scores in different questionnaires such as SADI (Villalobos et al., 2021), PCRS (Bivona et al., 2019; Ciurli et al., 2010), AQ (Bivona et al., 2008) or the Scale of Independent Behaviour (Trudel et al., 1998). On the contrary, no relationship was found between performance on the Trail Making Test with offline SA measured with the discrepancy in the PCRS (Bach &

David, 2006) or with measures of self-evaluation (measured with post-response confidence rating; Chiou et al., 2011). Positive correlations were also found between verbal fluency test in relation to offline SA when measured with the SADI (Villalobos et al., 2021; Wise et al., 2005) but a null relationship was found when offline SA was measured with discrepancy scores in the PCRS, AQ or DEX (Belchev et al., 2017; Caldwell et al., 2014; Morton & Barker, 2010). Verbal fluency has also been associated with emergent SA but not with other components of online SA such as self-regulation (Bettcher et al., 2008) or self-evaluation, with the latter being related only to tests measuring abstraction (Chiou et al., 2011).

Based on the revision of these studies, two main hypotheses arise. First, self-awareness seems to be related to specific aspects of EF and not to general executive impairment (Dromer et al., 2021b; Villalobos et al., 2021). Second, it is possible that different components of SA might be related to different components of EF. Therefore, in order to better understand the EF components that influence SA a more specific evaluation of EF and SA components is required (Chan et al., 2008; T. L. Ownsworth et al., 2002). Identifying in a more precise way the specific executive impairments that influence ISA is of paramount importance in order to propose rehabilitation strategies that directly address these components in a fine grained basis.

2.2.1. Specific executive functions processes related to self-awareness

In order to address the question raised above, we believe that experimental tasks can be more adequate tools for assessing the specific EF components that relate to specific SA components. In fact, different tasks derived from experimental psychology such as the Stroop task, go-no go task, visual search tasks etc., have been designed to isolate very specific aspects of EF.

However, very few studies have used experimental tasks to study specific aspects of EF in relation to offline and online SA. For example, McAvinue et al. (2005) used the Sustained Attention of Response Task (SART), a go-no-go task where no-go trials are predictable to study the relationship between emergent awareness (*i.e.* error detection) and sustained attention. These authors found a relationship between the amount of commission errors in the SART and emergent awareness in a sample of patients with traumatic brain injury. Similarly, (Dockree, Tarleton, et al., 2015; O'Keeffe et al., 2007a) found that commission errors in the SART correlated with online self-awareness, but not with offline self-awareness when measured with discrepancy scores in a metacognitive questionnaire. By contrast, commission errors in more complex versions of the go-no-go task, with more inhibition and working memory demands, significantly correlated with both online and offline awareness (Dockree, Tarleton, et al., 2015). These studies allowed identifying sustained attention and global inhibitory control (*i.e.* withholding a prepotent response) as executive components that could be involved in impaired SA. However, as we will address below other relevant executive components such as conflict monitoring have been neglected in relation to SA.

2.2.2. Relationship between conflict monitoring and self-awareness components

Since the first models of EF, such as the Norman & Shallice's (1986), EF are described as the processes activated in situations where more control is needed. Among these situations the authors consider conflict monitoring and resolution and error detection and correction (online components of SA) (Norman & Shallice, 1986; Posner & Rothbart, 1998; Shimamura, 2013). In addition, Shimamura (2000), in the dynamic filtering theory, proposes a direct link between conflict monitoring and metacognition. Based on the metacognitive model of Nelson & Narens (1990), the author proposes that the meta-level top-down control is applied by prefrontal cortex structures upon posterior brain structures responsible for the object-level processing. This control constitutes a filtering process that enables the selection of appropriate signals and the suppression of inappropriate ones, which is especially relevant when the monitoring process reveals a conflict at the object-level. Neuroimaging studies highly support this theory (Shimamura, 2000a).

Error detection theories also suggest a link between emergent awareness and conflict monitoring. The idea of the presence of a common mechanism between these two processes is mainly based on electrophysiological studies. Event related potential (ERP) studies identified a negative waveform that is generated 50-100 milliseconds after the commission of an error, the so-called Error Related Negativity (ERN) (Falkenstein 1990; 1991; Falkenstein et al., 2000; Gehring et al., 1993). The ERN is considered an index of error processing that, after the execution of the response, signals the presence of an error based on the mismatch between the representation of the performed incorrect response and the representation of the correct response (Carter & van Veen, 2007; Coles et al., 2001; Dehaene et al., 1994b; Falkenstein et al., 1991, 2000, 1995; Scheffers & Coles, 2000; Scheffers et al., 1996). Based on this first interpretation of the ERN, Yeung et al., (2004) set forth the "conflict theory" that formally and explicitly accounts for the similarity of error monitoring and conflict monitoring processes. The nucleus of this theory is that the conflict monitoring and error monitoring share a common mechanism based on the detection of a conflict. This idea principally comes from the similarities found, in experimental tasks, between the post-error ERN and other negative waveforms that are generated in presence of conflicting or incongruent information, such as the N400 and N2 (Falkenstein et al., 1991; Nick Yeung et al., 2004).

Conflict monitoring is usually studied with experimental interference tasks such as Flanker (Eriksen & Eriksen, 1974), Stroop (Stroop, 1935) and Simon (Simon & Berbaum, 1990) tasks. In these tasks participants have to respond as quickly and accurately as possible to the relevant dimension of the stimulus (*e.g.* the ink of the written word in stroop tasks) while ignoring the irrelevant dimension (*e.g.* the name of the color). However, the irrelevant dimension of the stimulus is usually automatically and rapidly processed (faster than the relevant dimension) (Carter & van Veen, 2007). In congruent trials the irrelevant and relevant dimensions of the stimulus are associated with the same (correct) response. On the contrary, in incongruent trials the irrelevant dimension of the stimulus is associated with the incorrect response, which, when activated, competes with the correct response associated to the relevant dimension, generating a *response conflict.*

ERP studies have identified a negative waveform (N2 in Flanker tasks and N450 in Stroop tasks) peaking roughly 250-450 ms after stimulus presentation, which has a greater amplitude during incongruent trials than congruent ones. These ERP are considered indexes of the detection of the conflict generated by the competition between the automatically activated incorrect response and the controlled activation of the correct response (Carter & van Veen, 2007; Larson et al., 2014). The ERN presents similar characteristics to these conflict monitoring ERPs. Both have a frontocentral distribution and dipole modeling has identified the anterior cingulate cortex (ACC), middle cingulate cortex (MCC) or presupplementary motor areas (pre-SMA) as their neural source (Dehaene et al., 1994a; Fu et al., 2023; Gehring et al., 2000; Holroyd et al., 1998; Nick Yeung et al., 2004). This shared source is also confirmed by fMRI studies that report enhanced ACC activation in response to correct responses in incongruent trial (compared to congruent trials) during interference and in trials with incorrect responses (Botvinick et al., 2001; Carter et al., 1998; Menon & Uddin, 2010; Nee et al., 2011; Shenhav et al., 2013; Ullsperger & von Cramon, 2006; Yeung et al., 2004). ACC activation during incongruent trials has been proposed to have the function of detecting the conflict during response selection. The detection of a conflict is used to signal the need for applying more control to the task (Botvinick et al., 2001; Yeung et al., 2004). Similarly, ACC activation in response to an incorrect response is proposed to have the function of detecting the conflict after response production. The detection of this conflict signals the need to implement more control in order to correct the error or avoid further errors (Carter & van Veen, 2007; Nick Yeung et al., 2004). Several studies have provided empirical data supporting the conflict theory of ERN. Some studies have demonstrated that the amplitude of the ERN is directly affected by the amount of conflict that is generated post-response (Danielmeier et al., 2009). Others have clearly demonstrated neural overlapping between the ERN and the N2 (Iannaccone et al., 2015). Finally, Yeung et al. (2004) have found significant correlations between the electrophysiological sensitivity to errors and to conflicts in healthy participants.

One conclusion we can draw from these studies is that conflict monitoring deficits may have a major role in some forms of anosognosia. Very few studies have explicitly investigated this hypothesis, providing evidence of an association between the Word-Color Stroop test and impaired offline SA (Bogod et al., 2003; Kashiwa et al., 2005). However, more research is still needed to further investigate the relationship of conflict monitoring with SA. In fact, the only two studies we are aware of using conflict tasks in relation to ISA looked at its relationship with patient alterations in offline SA. All the studies revised above and the conflict monitoring theory (Yeung et al., 2004) describe, both behaviorally and neurally, the relationship between conflict monitoring and error detection measured during the performance of a task. Therefore, conflict monitoring is also proposed to be a key mechanism involved in online SA, and more specifically in emergent awareness. Nevertheless, we are not aware of any study addressing this potential relationship.

In addition, these two studies used a single form of conflict task, the Stroop task. We wonder whether others sources of conflict arising at the response level, such as Simon interference, or from conflict with other distracting stimuli, such as in Flanker or visual search paradigms, could lead to similar or different patterns of relationship with SA. Several studies with healthy participants have directly compared different conflict tasks or combined them within the same task (Frings & Wühr, 2014; Frühholz et al., 2011; Funes et al., 2010; Kornblum et al., 1990; Korsch et al., 2014; Li et al., 2014; Nassauer & Halperin, 2003; Rey-Mermet & Gade, 2018; Rey-Mermet et al., 2019; Scerrati et al., 2017a). Most of these studies have found a behavioral pattern of additivity and independence to solve these different forms of conflicting situations, which has led researchers to conclude that they may tap into different mechanisms of cognitive control, implemented at different processing stages. Therefore, each conflict type may differ somehow in the locus where the conflict arises and, therefore, in the specific operations needed to detect the conflict and/or solve it (Stroop-like interference has been proposed to be solved by the excitatory biasing of task-relevant stimulus processing, whereas the Simon interference would require the inhibition of automatic response-priming processes) (Di Pellegrino, Ciaramelli, & Làdavas, 2007; Hochman, Wang, Milner, & Fellows, 2015; Maier, Di Gregorio, Muricchio, Di Pellegrino, & Harris, 2015; Picton et al., 2007; Stuss, Floden, Alexander, Levine, & Katz, 2001; Stuss et al., 1999; Swick & Jovanovic, 2002). Based on these studies, a straightforward question so far is whether the ability to monitor and solve different conflict types might be differently related to SA.

Finally, when the relationship between other components of EF (*i.e.* sustained attention) and online SA was investigated, the measure used for online SA was derived from experimental tasks (Dockree, Tarleton, et al., 2015; McAvinue et al., 2005; O'Keeffe et al., 2007a). However, as we will discussed in the next chapter, assessing online SA in naturalistic ecological tasks is important, as this could provide a more valuable index of SA and better mirror SA impairments that patients present in daily life. As far as we know, the relationship between specific conflict monitoring processes and online SA in naturalistic tasks has not been explored. In addition, finding a connection between conflict monitoring measures derived from an experimental task and online SA measured within ADL performance could constitute stronger evidence of shared cognitive processes involved in monitoring conflict and monitoring errors in daily life.

CHAPTER 3

Assessment of Self-Awareness

3.1 Assessment of offline self-awareness

Despite the high impact of anosognosia on independence, functional outcomes and the rehabilitation process, the awareness of deficits is widely neglected during patient's neuropsychological assessment. Even if the majority of clinicians consider self-awareness a paramount factor to evaluate, few health professionals actually include some standardized evaluation of self-awareness within the cognitive assessment protocol of acquired brain injury patients (Dromer et al., 2021a; Winkens et al., 2014).

When self-awareness is evaluated in clinical settings, the most used tools are interviews and questionnaires. Among them, The Self-Awareness of Deficits Interview (SADI; Fleming et al., 1996), the Awareness Questionnaire (AQ; Sherer et al., 1998) and the Patient's Competency Rating Scale (PCRS; Prigatano, 1996) are the most broadly used and with acceptable psychometric and conceptual properties according to recent reviews (Dromer et al., 2021a; Smeets et al., 2012). The assessment method used in these and other instruments is typically based on the discrepancy between patient's self-rating and the rating of a relative or the clinician about patients' functional problems (Dromer et al., 2021a; Prigatano et al., 1998). These questionnaires allow assessing a wide range of ADL domains and are very easy to administer, providing a quantitative index of patient's unawareness of deficits (*i.e.* more discrepancy = more severe unawareness of deficits) (Brown et al., 2021). However, one drawback of this type of assessment is that they are indirect measures, where the evaluation of patient's abilities and difficulties is not based on objective measures of patient's performance but on the report of a third person (*e.g.* a relative, a caregiver or a clinician). Therefore, factors such as the caregiver burnout and the familiarity with patient's current and previous level of functioning might affect the evaluation. As an example, it has been observed that relatives report more emotional and executive deficits than the clinicians do when rating patients' functionality (Caldwell et al., 2014; Malouf et al., 2014).

A method that might overcome the subjectivity problem inherent in the indirect informant-based assessment, although less used in clinical practice, is the performance-based discrepancy strategy. In this case the patient during a structured interview, is asked to rate their abilities/impairments in cognitive domains, such as memory, attention, orientation, speech, etc. This self-assessment about cognitive functioning is then compared with the patient's actual performance on neuropsychological tests assessing each cognitive domain (Anderson & Tranel, 1989; Brown et al., 2021; French et al., 2014; O'Keeffe et al., 2007).

Nevertheless, a major central issue of these assessment methods is that they exclusively take into consideration the offline component of self-awareness (*i.e.* metacognitive knowledge), assessing the patient's belief about their own abilities and difficulties (Brown et al., 2021; Winson et al., 2017). However, as outlined in the previous chapters, the impairment in the offline metacognitive knowledge might be caused by different underlying deficits related to online self-awareness components and/or to the updating (memory) process (Agnew & Morris, 2010; Toglia & Kirk, 2000). Therefore, the exclusive use of these tools tell us very little about what causes ISA in a given patient and which process or processes require intervention.

3.2. Assessment of online self-awareness

Online components of SA are mainly assessed in research settings. Methods used to assess anticipatory awareness and self-evaluation consist of asking the patient to estimate their performance in the incoming task and to rate their performance immediately after the completion of the task, respectively. The patient's estimation and rating of their performance are then compared with patient's actual performance (Ansell & Bucks, 2006; Berlingeri et al., 2015; Chiou et al., 2011; Fischer et al., 2004; Gilleen et al., 2014; Goverover, 2004; Stewart et al., 2010). The discrepancy between the patient's estimation of performance and the actual performance is considered an index of anticipatory self-awareness, reflecting the ability of the patient to predict the potential problems they might have during task performance. Similarly, the discrepancy between the patient's self-rating immediately after performance and the actual performance is an index of the self-evaluation component, assessing the ability of the patient to be aware of and report the problems faced during the performance. These methods of evaluation were firstly developed in metamemory research (Koriat, 2000; Nelson & Narens, 1990) and were then adapted to measure anticipatory awareness and self-evaluation in other cognitive domains such as attention, EF and perception (Chiou et al., 2011; Duke et al., 2002; Gilleen et al., 2014; Robertson & Schmitter-Edgecombe, 2015; Rosen et al., 2010; Sunderaraman & Cosentino, 2017a). In these studies the object of the pre/post evaluation is usually the participant's performance in traditional neuropsychological tests that assess the domain of interest.

Emergent awareness (*i.e.* error detection) and self-regulation (*i.e.* error correction) components are typically assessed online, while patients are engaged with a particular task (Prigatano & Sherer, 2020; Toglia & Goverover, 2022; Toglia & Kirk, 2000). Emergent awareness has mostly been investigated using experimental tasks such as Go/No-Go tasks (Dockree, Tarleton et al., 2015a; Hoerold et al., 2008; McAvinue et al., 2005; O'Keeffe et al., 2007a, 2007b). In these studies the participant has to verbalize or press a specific key when realizing that the previous key response to the task was an error (*i.e.* error detection). Self-regulation has been studied in experimental tasks assessing if the participant corrects a previous erroneous response (Ham et al., 2014). It has also been studied by measuring the post-error slowing effect (Rabbitt, 1966), which is a compensatory slowing of performance after error commission in order to avoid subsequent errors (Murphy et al., 2016; Purcell & Kiani, 2016).

These types of tasks offer the advantage of facilitating the evaluation of specific cognitive components that can be measured with great precision. Furthermore, they can be effectively combined with electrophysiological and neuroimaging technique (*e.g.* EEG and fMRI), which permits to gain an enhanced understanding of the cognitive processes of interest. Prior research employing these methodologies has successfully revealed impairments in online cognitive processes among patients with acquired brain injuries and neurodegenerative diseases (Chiou et al., 2011; Stephanie Cosentino et al., 2015; Di Pellegrino et al., 2007; Ham et al., 2014; Larson et al., 2006; Rosen et al., 2010; Wessel et al., 2014). This research also shed light on the possible underlying neural mechanisms involved in these processes, as we have explored in Chapter 2.

However, the use of experimental tasks and neuropsychological tests to assess the online components of self-awareness also entails some concerns. First of all, these tasks are completely new for the participant and are very different from the activities that the patients have to face in their everyday life. Neuropsychological and experimental tasks are characterized by the use of artificial stimuli and arbitrary stimulus-response associations, which are entirely unfamiliar to the patients. We should wonder whether the findings of ISA derived from these tasks are genuine or could be confounded by the fact that, due to the novelty of the tasks and potential difficulties in learning them, patients may have incomplete understandings of what "correct" means in the context of these new tasks. Similarly, patients' potential inability to accurately estimate how they will perform these tasks (*i.e.*, anticipatory awareness) might be influenced by their lack of prior experience with these tasks, making it challenging to anticipate the difficulties they might encounter. The absence of metacognitive knowledge about the task's characteristics and demands, as well as the correct approach to perform it, may hinder the patient's ability to accurately predict, monitor and evaluate the quality of their performance (Merchán-Baeza et al., 2020; Toglia & Kirk, 2000).

The use of artificial tasks might also compromise the validity of these measures for studying the potential relationship between online and offline self-awareness components. The research into the relationship among these components has reported controversial results, with some studies showing patterns of associations (Dockree, Connell, et al., 2015; Ham et al., 2014; Rotenberg-Shpigelman et al., 2014) and others of dissociations (O'Keeffe et al., 2007; Robertson & Schmitter-Edgecombe, 2015). A possible explanation for the inconsistent findings about online-offline relationship might be the fact that the measures of online and offline awareness focus on very different domains (Merchán-Baeza et al., 2020; Toglia & Goverover, 2022). While metacognitive questionnaires measure self-awareness by asking for functional and familiar tasks, online self-awareness is mainly assessed with artificial, novel tasks (Al Banna et al., 2016; Fleming et al., 1996; Godfrey et al., 1993; Ownsworth et al., 2000; Prigatano et al., 1998; Sherer et al., 1998). Furthermore, while measures of offline SA, usually ask for a wide range of functional domains (including behavioural, cognitive and social components), the online measures described above assess self-awareness in isolated and specific cognitive domains. However, as it has been previously proposed, self-awareness seems not to be a global process but different levels of SA can be found depending on the domain that is being considered and the characteristics of the task that is being performed (Chen & Toglia, 2019; Chudoba & Schmitter-Edgecombe, 2020; Fitzgerald et al., 2017; Fleming et al., 2014a, 2014b; Toglia & Goverover, 2022).

In conclusion, obtaining valuable indexes of online self-awareness components from these measures can be problematic. As we will fully describe below, one potential solution to all the problems reported above may come from the using of an evaluation protocol based on structured observation of well-known Activities of Daily Living (ADL) to measure the online components of SA.

3.3. Online self-awareness evaluation in the context of activities of daily activities

3.3.1. Toward a more ecological assessment of cognition

A growing line of research from the Neuropsychology and Occupational Therapy fields has highlighted the importance of enhancing the ecological validity of the assessment of the various cognitive domains (Azouvi, 2016; Baum et al., 2008; Chan et al., 2008; Chevignard et al., 2008; Pinto et al., 2023; Spooner & Pachana, 2006; Wilson, 1993). To do so, several authors have designed different ADL-based evaluation tools that try to reproduce in the laboratory well-known everyday actions (see Romero-Ayuso et al., 2019 for a recent review).

Before reviewing these tools, let’s define what ADL are. The term “ADL” encompasses a multifaceted spectrum of activities that respond to different human needs (Moruno, 2006).

For example, some ADL address physiological needs that must be met for survival. Examples of these activities are eating, drinking, going to the bathroom and sleeping. There are other ADL that are not essential for immediate physiological survival but play a crucial role in self-care and overall health. These activities include dressing, brushing teeth, and taking showers. All these types of ADL fall under the broader concept of Basic Activities of Daily Living (BADL). On the other side, other more complex ADL are referred to as Instrumental Activities of Daily Living (IADL). IADL, such as shopping, meal preparation, event planning, and the like, are distinguished by the fact that they are not ends in themselves, but rather serve as instruments to facilitate the accomplishment of other ADLs (Moruno, 2006). Performing ADL does not only confer autonomy and self-maintenance, but additionally allows people to participate in society, defining and expressing their identities and values (Kielhofner, 2002; Moruno, 2006). Based on that, it is not surprising that the level of ADL independence has shown to be a key index of people's quality of life and mental health (Albanese et al., 2020; Haghgoo et al., 2013; Pusswald et al., 2015). For these reasons a better knowledge of the processes involved in ADL as well as developing new tools to assess and rehabilitate ADL performance after neurological disease constitute a main objective in research and clinical settings.

Beyond this categorization, all ADL are dynamic activities that require interaction with several objects and where the actions and the objects to be used are usually well-known. Besides, one main property of ADL is that they require sequencing of a series of action steps in order to complete the task (Doig, Fleming, Ownsworth, et al., 2017; Moruno & Romero, 2005). Apart from the obvious implication of sensorimotor processes, ADL requires the implication of numerous cognitive processes. For example, when shopping, we have to recognize among the cards we have in our wallet which is the one for payment;

we have to remember all the steps of the task and perform them in the correct order (*e.g.* select the item → go to the checkout counter → take the card out of the wallet → swipe or insert the card in the card reader, etc.); we need to recall all the items on our shopping list and inhibit the impulse of buying any additional items that might capture our attention.

Given the variety of cognitive process involved in ADL performance different types of action errors may emerge. These include object substitution errors, where the wrong object is used for an action (*e.g.*, stirring coffee with a fork); visuospatial errors, related to the improper orientation of an object in relation to the hand or to another object; sequential errors, which include omissions, repetition, sequence violation, and addition errors. Omission errors occur when a necessary step is missed, repetition errors involve unnecessary repeated steps, sequence violation errors result from altering the logical order of steps, and addition errors entail performing extra, irrelevant steps (*e.g.* adding a teabag to coffee) (Giovannetti et al., 2008; Morady & Humphreys, 2009; Norman, 1981; Reason, 1979; Schmitter-Edgecombe et al., 2021; Schwartz et al., 1991). Several authors have proposed different structured ADL tasks to assess the cognitive processes involved in daily activities (Buxbaum, 1998; Chudoba & Schmitter-Edgecombe, 2020; Giovannetti et al., 2008; Schmitter-Edgecombe et al., 2021; Schmitter-Edgecombe & Parsey, 2014; Schwartz et al., 1998, 2002b; Toglia, 2015). Most of the studies using these ADL-based tools try to find relationships between error types and the execution in traditional neuropsychological tests to reveal if different types of errors underlie different cognitive processes (Giovannetti et al., 2006, 2008; Schwartz et al., 1995; Toglia, 2015). This line of research has led to the development of the influential "Omission-Commission" model (Giovannetti et al., 2008). This model proposes that the two categories of errors might tap into different cognitive processes, with omissions (the failure to perform a necessary action) being related to general cognitive and episodic memory impairments and commission errors (the performance of an incorrect action, including sequence violation, object substitution and step repetition) is associated with by EF impairments (Giovannetti et al., 2012; Giovannetti et al., 2008, 2006).

Other researchers have reported that the characteristics of the task (*e.g.* dual task performance) can influence the types of errors exhibited by participants (Forde & Humphreys, 2000; Forde et al., 2004; Giovannetti et al., 2007; Morady & Humphreys, 2009)(see reference). For instance, Morady & Humphreys (2009) observed, during the performance of ADL-based tasks of a patient with ABI and action disorganization syndrome, an increase in the proportion of omission errors when semantically-related distractors were introduced into the task. However, the proportions of other error types, such as sequence violations, repetitions, and additions, remained unaffected.

These studies show how ADL-based tasks can be good tools to directly assess specific cognitive impairments after brain disease in a more ecological basis than traditional ones (Salazar-Frías et al., 2023; Schmitter-Edgecombe et al., 2021). Besides, with the observation of different patterns of errors in a given ADL it may be possible to evaluate different cognitive processes simultaneously.

3.3.2. Activity of Daily Living-based tasks to assess online self-awareness

More relevant to the present dissertation, this type of ADL-based assessment tools has also been shown to be useful for studying and assessing online SA. Several authors have proposed a coding system to identify errors that were detected and corrected, based on participants' verbalizations and behavioral attempts to remedy the errors. Using this strategy, Giovannetti et al. (2002) studied error detection in relation to different types of errors during the performance of three ADL tasks (*i.e.* prepare a coffee with milk and a butter and jelly toast; wrap a gift and pack a lunch box; shortened version of the Multi-Level Action Test, see Table 3.1). The authors reported that participants (*i.e.* patients with dementia as well as healthy controls) were more aware of object substitution and sequence violation errors than of omissions or addition errors.

Other studies using ADL-based tools have found that error detection and correction abilities seem to be affected by the complexity of the ADL task, with a larger amount of detected errors in simpler ADL conditions compared to more complex ones (Morady & Humphreys, 2009; Rotenberg-Shpigelman et al., 2014). Therefore, and in line with the previous argument, evaluating emergent awareness and self-regulation within the context of ADL seems to constitute an opportunity to evaluate detection abilities in response to various error types and ADL types, which may lead to a more comprehensive understanding of these components.

Even more relevant, due to the high familiarity of ADL, there is an increased probability that participants have already strong memory representations of how to perform the task correctly. The fact that participants have that knowledge ensures that the estimation of their performance (*i.e.* anticipatory awareness), the detection of errors during the performance (*i.e.* emergent awareness) or the post-evaluation of the performance (*i.e.* self-evaluation) can be done by comparing it with rich representations of the task in its correct form. Therefore we can be more confident that the deficit found in any of these components will be due to genuine problems in online SA, and not confounded with lack of task knowledge (which is more probable with novel tasks such as experimental tasks or neuropsychological tests, as stated above). Finally, it has been suggested that because ADL hold particular significance for patients, they are more likely to be interested and motivated during task performance, aspects that are supposed to affect self-monitoring (Robertson & Schmitter-Edgecombe, 2017; Romero-Ayuso et al., 2019; Toglia & Kirk, 2000).

Based on these arguments, several studies have developed new assessment tools within the context of familiar and significant ADL. These tools have demonstrated validity for studying online SA in a wide range of populations: healthy adolescents, young and older adults, patients with mild cognitive impairments, dementia, multiple sclerosis and ABI (Arora et al., 2021; Bettcher et al., 2008; Casaletto et al., 2016; Chen & Goverover, 2021; Chudoba & Schmitter-Edgecombe, 2020; Doig, Fleming, & Lin, 2017; Doig, Fleming, Ownsworth, et al., 2017; Giovannetti, Libon, & Hart, 2002; Giovannetti et al., 2007; Goverover et al., 2014, 2020; Hart et al., 1998; Jaywant et al., 2022; Rotenberg-Shpigelman et al., 2014; Schmitter-Edgecombe et al., 2021; Seligman et al., 2014; Zlotnik & Toglia, 2018) Table 3.1 describes the naturalistic tasks that have been proposed to measure online SA components. The table indicates which online components are measured in each study and whether measures or offline SA were or were not included.

Table 3.1 ADL-based tools to assess online SA components (adapted from Toglia & Goverover, 2022)

ADL task description	Author (year)	Offline component measures	Online awareness component measures
Multilevel Action Task/Naturalistic Action Test Three everyday tasks with different level of difficulty: 1- Making a toast with butter and jelly and a coffee with cream and sugar. 2- Wrapping a present. 3- Prepare a lunch-box.	Hart et al. (1998)	No offline	**Emergent awareness**: % detected errors **Self-regulation:** % corrected errors **Self-evaluation:** self-rating questionnaire about cognitive behaviours during task performance.
	Giovannetti, Libon, & Hart (2002)	IADL-PSM: self-informant discrepancy	**Emergent awareness**: % detected errors **Self-regulation:** % corrected errors
	Bettcher et al. (2008)	No offline	**Emergent awareness**: % detected errors **Self-regulation:** % corrected errors
Coffee Challenge Participant has to make two different cups of coffee with creamer and sweetener.	Giovannetti et al., (2007)	No offline	**Emergent awareness:** % detected errors
Day Out Task/Night Out Task Preparing for a day/night out with a friend performing eight subtasks: collect change, plan a route bus, prepare a tea to go, locate a recipe and collect the ingredients, collect a snack to go, pack all items, make a phone call.	Schmitter-Edgecombe et al. (2021)	No offline	**Self-regulation:** self-correction.
	Chudoba & Schmitter-Edgecombe (2020)	No offline	**Anticipatory**: discrepancy between prediction and actual performance. **Self-evaluation**: discrepancy between self-rating and actual performance. **Updating:** predict performance in a similar task 40 minutes after the completion of the task
Occupation-Based online awareness assessment: Multistep tasks selected based on the significance for the patient: 1- Use of an i-Pad application to produce music 2- Make an hot drink 3- Prepare a simple hot milk 4- Plan and write a shopping list 5- Complete a weekly timetable with a list of activities.	Doig, Fleming, & Lin (2017)	No offline	**Self-regulation:** total amount of self-corrected errors
	Doig, Fleming, Ownsworth, et al., (2017)	AQ; SADI	**Self-regulation:** total amount of self-corrected errors
Weekly Calendar Planning Activity Scheduling in a weekly timetable a list of 10/18 (depending on the version) to do activities, while following some rules.	Goverover et al., (2020)	No offline	**Emergent awareness:** % of detected errors **Self-evaluation:** discrepancy between self-rating of the task and actual performance.
	Arora et al., 2021)	No offline	**Emergent awareness:** % of detected errors **Self-evaluation:** discrepancy between self-rating of the task and actual performance.
	Jaywant et al., (2022)	No offline	**Emeregent awareness: error detection (% detected errors)** **Self-evaluation:** discrepancy between self-appraisal of the task and actual performance
	Zlotnik & Toglia, (2018)	Metacognition index del BRIEF	**Self-evaluation**: discrepancy between post-evaluation and performance

Actual Reality Task Use of computer to access internet and purchase: - An airline ticket - Cookies for a present	Goverover et al., (2014)	FBP: self-informant discrepancy	**Anticipatory**: discrepancy between prediction and actual performance. **Self-evaluation**: discrepancy between self-rating and actual performance.
	Chen & Goverover, (2021)	MMS, FBP; SP: self-informant discrepancy	**Anticipatory**: discrepancy between prediction and actual performance. **Self-evaluation**: discrepancy between self-rating and actual performance.
Three ADL task - Upper body dressing - Drink preparation - Telephone use to obtain information	Rotenberg-Shpigelman et al., (2014)	ISA scale: clinician rating	**Self-evaluation**: after the completion of the task the participant rates their performance
Everyday Multitasking Test: Complete as much as possible 4 tasks in a 12-minutes timeframe - Cooking a Meal - Advanced Finances - Medication Management - Telephone Communication.	Casaletto et al., (2016)	Everyday Functioning questionnaire	**Anticipatory**: discrepancy between prediction and actual performance. **Self-regulation:** % corrected errors **Self-evaluation:** discrepancy between self-rating and actual performance.

AQ = Awareness Questionnaire; BRIEF = ;FBP = Functional Behaviour Profile; IADL-PSM = Instrumental Activities of Daily Living and Physical Self-Maintenance Scales; MMS = Money Management Survey; PSM = SADI = Self-Awareness of Deficits Interview; SP = Sensory Profile

Some of the assessments of Table 3.1 focus on error detection and correction abilities during task execution, while others evaluate anticipatory and self-evaluation SA before and after task performance. For example the Occupation-Based online awareness assessment (Doig, Fleming, & Lin, 2017) studied error behaviours in TBI and dementia patients and identified self-correction impairments compared to healthy controls. Nevertheless, this kind of evaluation does not allow differentiating emergent awareness and self-regulation components, combining them into the same index. Emergent awareness and self-regulation are dissociated and evaluated separately in several studies from Giovannetti's laboratory (Bettcher et al., 2008; Giovannetti, Libon, & Hart, 2002; Seligman et al., 2014). In these studies error detection and correction are assessed during task performance through a sophisticated coding system. This method has been mostly used for assessing these components of online awareness in patients with neurodegenerative diseases and only one study evaluates emergent awareness and self-regulation separately in a TBI sample (Hart et al., 1998). In addition, in all these studies, measures to evaluate the other online components of SA, such as anticipatory awareness, self-evaluation and/or updating components were not used. These latter components were evaluated in Chudoba et al. (2020), however in this case emergent awareness and self-regulation during the task were not assessed. Therefore, we can conclude that we are still missing an evaluation protocol that would allow assessing all and each of the components of online SA as well as the updating component in the context of naturalistic, familiar ADL.

In addition, very few studies have measured the relationship between online and offline components all within the context of the same domains (*i.e.* ADL). Giovannetti et al. (2002) analyzed emergent and self-regulation in relation to the offline SA component in a sample of patients with mild cognitive impairments, finding no relationship among them. However, anticipatory or self-evaluation processes were not evaluated. On the other side, Rotenberg-Shpigelman et al., (2014) did find significant moderate correlations between offline awareness and self-regulation and self-evaluation, but error monitoring abilities during task execution were not evaluated. Finally, Goverover et al. (2014) found no relationship between anticipatory awareness or self-evaluation components and offline SA. Therefore, it is possible that some online components are related to offline metacognitive awareness while others are not. More research is needed where all online components proposed by the DCMA model are measured within the context of ADL functioning and systematically compared with functional offline measures of SA.

Some other issues should be noted in reference to the studies in Table 3.1. First of all, only few of the ADL-based tests used to assess online SA have been formally validated (Giovannetti, Libon, Buxbaum, et al., 2002; Schmitter-Edgecombe et al., 2021; Schwartz et al., 1998, 2002; Toglia, 2015) and as far as we know only one has been validated in the Spanish population in our lab (Salazar-Frías et al., 2023). Given the importance that cultural aspects have on ADL performance, ADL-based assessment tools should be systematically adapted to and validated in different cultures.

In addition, most of the validated tests consist of ADL which are instrumental in nature, and that have high planning, working memory and multitasking demands (Chudoba & Schmitter-Edgecombe, 2020; Schmitter-Edgecombe et al., 2021; Toglia, 2015). These conditions could be especially useful for studying high level processes and SA in participants with mild cognitive alterations (*e.g.* elderly, mild cognitive impairments of ABI patients) (Schmitter-Edgecombe et al., 2021; Zlotnik & Toglia, 2018). However, they also considerably increase the complexity of the task, which might hamper online SA assessment in patients with more severe cognitive impairments.

Finally, one of the primary drawbacks related to ADL-based evaluation resides in the difficulty of scoring all the possible behaviors and errors that the patient may exhibit. The observation and codification of all the spontaneous behaviors that patients might produce is very effortful and time-consuming. To do so, participants' performance usually must be video-recorded in order to be codified and scored offline by the evaluator/s. These characteristics, apart from discouraging the use of ADL-based measures in research settings, largely hinder the application of these types of tools in clinical settings (Giovannetti et al., 2019).

From our laboratory we have recently proposed an evaluation protocol to assess online SA in the context of ADL in patients with ABI (Merchán-Baeza et al., 2020). This protocol has been designed in order to overcome some of the issues reported above. The protocol includes measures of all online SA components (*i.e.* anticipatory awareness, emergent awareness, self-regulation and self-evaluation) as well as a measure of the updating process described in most SA models. All these components are assessed in the context of two ADL, one basic and one instrumental ADL, which were manipulated by including semantically-related distractors and conflicting situations (*i.e.* problematic situations that the patient has to resolve in order to successfully complete the task).

The inclusion of a basic and an instrumental ADL responded to the need of designing an assessment tool that permitted a more exhaustive evaluation of patients' online SA. In fact, as stated above, SA depends on the characteristics of the task performed and previous studies demonstrated that different SA levels might be found for more complex instrumental ADL and simpler basic ADL (Rotenberg-Shpigelman et al., 2014; Salazar-Frías et al., in press). In addition the inclusion of a basic ADL in the protocol allows the evaluation of online SA in more severely affected patients. The reasons for including the distractors and conflicting situations are threefold. Firstly, due to these manipulations the ADL tasks of the protocol resemble more closely the real world. In fact, usually the objects required to perform the task are found among other numerous unnecessary objects and are not ready-to-use. Secondly, the inclusion of these manipulations increases the executive and monitoring demands of the tasks without excessively increasing their complexity in terms of planning and multitasking. Finally, all the patients have to face the same problems during the tasks, which create a closed number of observable behaviors of error detection and correction. Evaluating patient's performance focusing only on these behaviors might be a method that permits to simplify the scoring of ADL-based emergent awareness and self-regulation. As we will see in Chapter 6 preliminary data of the validity of this protocol will constitute one of the empirical chapters of the present thesis.

CHAPTER 4

Neuroanatomical Correlates

of

Self-Awareness

4.1. Neural bases of offline self-awareness

Given the association between reduced awareness of deficits and EF previously described, it has been widely suggested that the frontal lobe might be especially relevant for SA (Prigatano & Sherer, 2020). Empirical studies using structural and functional neuroimaging confirmed the relationship of medial and lateral prefrontal structures with offline SA in patients with neurodegenerative diseases (Amanzio et al., 2011; Hanyu et al., 2008; Harwood et al., 2005; Ries et al., 2006; Salmon et al., 2005; Schmitz et al., 2006; Sedaghat et al., 2010; Shibata et al., 2008; Zamboni et al., 2013) and ABI (Bivona et al., 2014; Hoerold et al., 2013; Schmitz et al., 2006). However, other authors have proposed that different brain regions, instead of merely frontal areas, might be related to anosognosia (FitzGerald et al., 2012; Prigatano & Schacter, 1991; Taylor et al., 2007). Empirical research supported this view, finding that also temporal, parietal and subcortical regions show association with offline SA (Amanzio et al., 2011; Hanyu et al., 2008; Salmon et al., 2005; Sedaghat et al., 2010; Tondelli et al., 2018; G. Zamboni et al., 2010). In addition, Prigatano (2009) suggests that different forms of anosognosia could be related to lesions in different neural networks. To investigate this proposal, a more exhaustive evaluation of the neural mechanisms related to the online components of self-awareness is still required.

4.2. Neural bases of online self-awareness

4.2.1. Neural bases of anticipatory awareness and self-evaluation components

Several studies investigated brain areas associated with anticipatory awareness and self-evaluation. Lesion studies helped to find neural dissociations between these components, with focal lesion in the medial prefrontal area leading to selective impairments in anticipatory awareness and self-evaluation being more related to dorsolateral prefrontal lesions (Pannu et al., 2005; Schnyer et al., 2004).

The involvement of different areas in these two components was also documented in structural and functional neuroimaging studies. In these studies, both anticipatory and self-evaluation components were found to be related to medial structures of the brain in the prefrontal, temporal and parietal regions (Berlingeri et al., 2015; Chua et al., 2009) (Garcia-Cordero et al., 2019; Grossner et al., 2018; Mimura & Yano, 2006; Rosen, 2011; Schmitz et al., 2006; Tondelli et al., 2018). Nevertheless, additional areas emerged as related to self-evaluation components in lateral structures such as the dorsolateral and ventrolateral prefrontal cortex (Fleming & Dolan, 2014; Grossner et al., 2018; Leonesio & Nelson, 1990; Miner & Reder, 1994; Nelson & Narens, 1994). These studies support the idea that different self-awareness components might be related to different neural circuits.

Interestingly, not only different online components of SA are related to different neural networks, but also SA in different domains seems to depend on different cerebral areas. Tondelli et al. (2018) found that grey matter volume in the right medial temporal lobe was associated with self-evaluation of performance independent of the task domain. However, the authors found that self-evaluation of performance on different neuropsychological tests was also selectively associated with the grey matter volume of the areas directly related to the process involved in the task (*i.e.* left hippocampus and amygdala for the episodic memory test, precuneus and lateral occipital cortex for visuospatial tests and the ACC, precentral gyrus and orbital cortex for EF tests). Therefore it is likely that the self-evaluation component is supported by an interaction between areas specifically related to the process of recalling task performance (*i.e.* short-term memory) and areas related to the process object of the evaluation itself (Soto et al., 2018; Tondelli et al., 2018). This finding also supports the idea that metacognition can be domain-specific (Fitzgerald et al., 2017; Fleming et al., 2014b) and highlights the importance of task selection when measuring online self-awareness components.

4.2.2. Neural bases of emergent awareness

Neural mechanisms of emergent awareness were studied in several EEG studies within the context of experimental tasks, observing the ERN component previously mentioned. Neuroimaging studies with healthy population and with brain injury patients identified mainly two areas in the prefrontal cortex associated with this process, specifically the ACC and the dorsolateral prefrontal cortex (PFC). Lesion based studies reported that acquired brain injury patients with lesion in one of these two areas show altered ERN after errors (Gehring & Knight, 2000; Maier et al., 2015; Modirrousta & Fellows, 2008; Stemmer et al., 2004; Wessel et al., 2014). However, the results of some behavioural studies suggest that areas outside the prefrontal lobe might also be involved in error detection. For example, Hoerold et al. (2013) found that patients with lesion in the frontal lobe and patients with lesion sparing frontal areas showed impaired error detection (measured with verbalizations of the commission of an error). Similarly, (Dockree, Tarleton, et al., 2015) found no differences in error detection between patients with frontal lesion and patients with lesion in posterior areas (Dockree, Connell, et al., 2015; Hoerold et al., 2013). In addition patients with medial or lateral prefrontal lesion, even showing an altered ERN pattern, preserved the ability to explicitly reporting the commission of an error (Maier et al., 2015; Modirrousta & Fellows, 2008; Stemmer et al., 2004; Wessel et al., 2014).

The involvement of posterior areas in error detection can be understood introducing another ERP component, the post-error positivity (Pe). The Pe usually emerges around 200-400 ms after the commission of an error (Falkenstein et al., 2000; Overbeek et al., 2005) and seems to represent a different neural process than the one represented by the ERN. Meanwhile the ERN seems to represent the detection of a conflict that signals that something wrong has occurred during the performance, the Pe represents the evidence accumulation process that leads to the conscious identification of the error (Di Gregorio et al., 2016; Gibbons et al., 2011; O'Connell et al., 2007). Indeed, while the ERN has been found after both, errors that were verbally reported and unreported errors, the Pe was only found after explicitly reported errors (Di Gregorio et al., 2016; Hoonakker et al., 2016; Kieffaber et al., 2016; O'Connell et al., 2007). In contrast to the ERN, that has a centrofrontal source, the source of the Pe has been identified in the centroparietal area. Neuroimaging studies have also identified this dissociation, with medial prefrontal areas being involved in both types of errors (*i.e.* conscious and unconscious) and posterior areas, such as the insula and the parietal cortex, responding specifically to error that are consciously recognized (Agam et al., 2011; Fiehler et al., 2004; Hester et al., 2005; Klein et al., 2007; Orr & Hester, 2012).

The involvement of the insular and/or parietal cortex in the process of evidence accumulation subserving error detection has been found regardless of the stimulus modality used in the task (Murphy et al., 2015; Nieuwenhuis et al., 2001; O'Connell et al., 2007; Shalgi et al., 2009). However, it is probable that, as seemingly occurs with self-evaluation, error recognition also requires the involvement of additional specific areas that vary depending on the type of error that has to be detected.

4.3. Neural mechanisms of emergent awareness in Activities of Daily Living

4.3.1 Qualitative neural differences in error detection

In the previous chapter has been proposed that different types of errors and different pattern of errors commission are related to different cognitive processes. However, qualitative differences between error types were not only found when studying their neuropsychological predictors, but also when investigating the neural mechanism relating to each error type, although we are aware of very few studies that have studied this (Bailey et al., 2013; Seidel et al., 2013). For example, Bailey et al. (2013) scored the amount of omission, commissions and off-tasks addition errors committed by participants with dementia while performing the NAT (see Table 3.1). The authors, using voxel based morphometry (VBM) technique, found neural support for the Omission-Commission model (Giovannetti et al., 2008), with different cerebral areas being related to each category of errors. In fact, while the volume of medial temporal lobe was related to omission errors, the volume of the dorsolateral PFC was related to commission errors and off-task additions were related to the volume of the ACC.

Another idea emerging from the behavioural studies described in the previous chapter is that the process of error detection varies depending on the type of error assessed (Giovannetti, Libon, & Hart, 2002). This specificity was also identified in several functional neuroimaging studies, with different cerebral areas responding to the detection of different types of observed ADL errors. For example, Manthey et al. (2003) show participants short videos with simple ADL actions (*e.g.* fold napkin) that might contain an object substitution error or a visuospatial error. The authors found that several areas in the brain responded to both types of errors when compared to baseline aimless object manipulation. However some areas differed between the two conditions, with the left premotor area specifically responding to object substitution errors and bilateral superior frontal gyrus, right anterior inferior parietal surcus, middle temporal gyrus and bilateral thalamus responding to visuospatial errors. Similarly, Weiss et al. (2006) compared the observation of ADL videos containing sequence violation errors (*e.g.* drink before filling the glass with water) or visuospatial errors (*e.g.* pour water next to the glass) to baseline condition (*i.e.* task instruction). These authors also found that the right parietal cortex was related to spatial errors, whereas medial prefrontal activation in the ACC supported observation of sequence violation errors. All these studies confirm that different neural circuits are related to the detection of different types of ADL errors.

4.3.2. Sequence knowledge and sequence error monitoring

As described earlier, one of the distinctive characteristics of ADL is the need to perform multiple actions and steps to complete the task. This characteristic makes sequence knowledge about the task one of the most critical components of ADL (Botvinick & Plaut, 2004). Indeed, performing all the required steps in an adequate order is essential to achieve the final goal. The interest of studying sequence aspect of ADL in relation to online SA is based on the fact that, as pointed in Chapter 3, several errors may emerge when the sequential performance of ADL steps is altered. In addition, sequence errors such as omissions, repetition and order violation are among the types of errors most frequently observed during the ADL performance in both healthy controls and patients with neurological diseases (Giovannetti, Libon, Buxbaum, et al., 2002; Norman, 1981; Reason, 1979, 1989; Schwartz, 2006). Although these errors all arise due to the alteration of the adequate sequence of steps, they are different sequence errors with specific characteristics. Therefore, different processes may be involved not only in their production but also in their detection. The studies previously revised found a neural dissociation between omission and commission errors during ADL performance (Bailey et al., 2013; Seidel et al., 2013). However, in the latter category different types of sequential and non-sequential errors were included. Furthermore, these studies focused on the error pattern committed by the participants and their neural mechanisms, but the neural correlates of detecting and recognizing different types of errors were not studied. On the other hand, the studies that investigated the brain areas involved in the recognition of different types of errors mainly focus on differences between sequence violation errors and non-sequence errors (*i.e.* object substitution and visuospatial errors; Manthey et al., 2003; Weiss et al., 2006). Therefore, it is still unexplored whether the recognition of different types of sequence errors, despite all types representing failure of sequence knowledge and sequence monitoring, depends on different brain networks.

Another important aspect related to sequence errors that cannot be studied in the context of other types of ADL errors is the influence that expectation has on ADL monitoring and error detection. Sequence knowledge is hypothesised to be hierarchically organized (Botvinick, 2008; R. Cooper & Shallice, 2000; Lashley, 1951; Schwartz, 2006). The task goal is at the top of the hierarchy, branching to several subgoals at the intermediate level. In turn, each subgoal branches to more and more discrete actions, with the lowest level containing the action needed to directly manipulate the objects (Cooper & Shallice, 2000). See figure 4.1 for an example of the ADL hierarchical tree of action for a tea-making task.

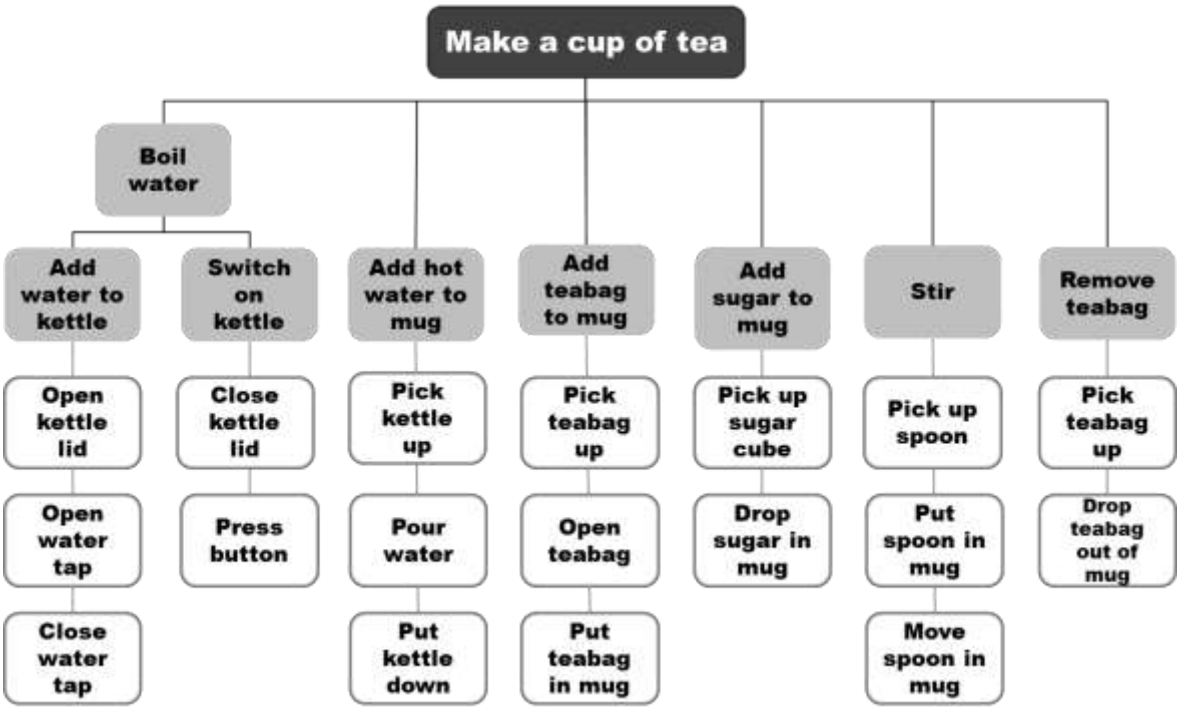


Figure 4.1. Example of the hierarchical structure of the sequence of steps to perform the task of making a cup of tea

Looking at the subgoal level of the hierarchy tree represented in Figure 4.1 it is evident that some of the steps must necessarily be performed in a determined order, while other steps can be performed at any point in the sequence without altering the final outcome. For example, the step “add hot water to the mug” must necessarily be performed after boiling the water, and “switch on the kettle” after the step “add water to kettle”. Therefore, if the sequence of steps is “add water to kettle” → “switch on the kettle” → “add hot water to mug”, each subsequent step is usually highly expected to follow the preceding one, being somehow predictable. On the other hand, steps like “add sugar to mug” and “add milk” can be performed at any point (or not be performed at all if the final goal is, for example, to make a black tea). Therefore, this kind of steps is not so predictable, since many different options of sequence including these steps are correct. Interestingly, Holroyd & Yeung (2012) propose that an additional function of the ACC, a part of error and conflict detection described before in this introduction, is the selection and maintenance of action options. The authors reported that ACC activity is more pronounced when the task presents several response options than when the options are constrained (Holroyd & Yeung, 2012a). Therefore, a suggestion arising from this theory is that the ACC should be less involved in the monitoring of highly predictable steps compared to low predictable steps.

Furthermore, action predictability might have a relevant role in error detection. In line with this, it has been shown that it is easier to detect an error when it does not follow our expectation (Berger & Posner, 2023; Meijs et al., 2018; Sellen, 1994). Besides, some errors, such as step repetitions and sequence violation can be considered as surprising and unpredictable events that break down the observer expectations. Empirical research also supports this view. In fact, Schiffer et al. (2014), reported medial prefrontal activation in the dACC in response to both unexpected correct actions and unexpected erroneous actions. The authors suggest that the ACC activation usually found in response to errors might be reflecting the detection of an unexpected event. The involvement of the same cerebral area in the detection of errors and unexpected events suggests that these two processes might share cognitive mechanisms. As a conclusion, steps predictability is a relevant aspect of ADL sequence monitoring and might be involved in the process of error detection. However, to the best of our knowledge, no studies to date have explicitly investigated whether different brain networks are involved in monitoring different ADL steps based on their predictability and whether the monitoring of correct unpredictable steps and erroneous steps are supported by similar neural networks.

Understanding whether different neural mechanisms are involved in the monitoring of highly predictable and low predictable steps might be helpful to better understand the behavioural pattern of neurological patients in a clinical setting. For example, the evaluation of the ability of the patient to monitor highly vs. low predictable steps could be show different patterns of execution and be used as an index, in order to have a more comprehensive insight into the cognitive impairments that are affecting performance (*e.g.* monitoring vs. semantic knowledge).

PART II

AIMS OF THE RESEARCH

CHAPTER 5

Motivation and Aims

In the previous chapters a comprehensive revision of anosognosia as a neuropsychological disorder has been put forward, revisiting the theoretical models and empirical studies that strengthen the understanding of this multicomponential construct. The different components of SA have been introduced and it has be highlighted the importance of the assessment of all and each of them to obtain an exhaustive picture of patients unawareness of deficit. Finally the cognitive mechanisms underlying SA, with the focus on EF and among them a special interest in conflict monitoring, and the neural basis of different components of online SA were described. However, throughout the introductory chapters were also pointed out various aspects of the study of ISA that still need more research.

The general concern within the ISA-related literature relies on the necessity to improve the assessment of SA for both research and clinical purposes. Several factors drive this need. A first issue is that usually, when assessing ISA in neurological patients only the offline component of SA is taken into consideration (Al Banna et al., 2016; Brown et al., 2021). However, as reported in Chapter 1, several forms of anosognosia can be observed depending on which specific component is affected (*e.g.* emergent awareness, self-evaluation or updating components) (Crosson et al., 1989; Hannesdottir & Morris, 2007; Morris & Hannesdottir, 2004; Toglia & Kirk, 2000). Consequently, a comprehensive evaluation of all the online components of SA, and the updating component, is necessary in order to have a comprehensive understanding of the cognitive problems that are mainly affecting SA in each patient.

A second issue is tied to the type of tasks and tests typically employed in the assessing of online SA. Indeed, methods for online SA assessment (primarily used in research settings) typically rely on evaluating patients' estimation, monitoring, and self-evaluation of their performance in neuropsychological tests and experimental tasks (Chiou et al., 2011; Duke et al., 2002; Gilleen et al., 2014; Robertson & Schmitter-Edgecombe, 2015; Rosen et al., 2010; Sunderaraman & Cosentino, 2017a). However, as stated in the introduction, these tasks may lack of ecological validity, since they are usually new for the patients and different in nature from the tasks that they have to face in their daily life. It is widely suggested that SA is domain-specific and, consequently, it may dependent on the type of task and degree of familiarity (Toglia & Goverover, 2022). In line with this, assessment tools based on well-known and familiar ADL might be more suitable for evaluating SA, in order to gain a deeper understanding of how ISA impacts patients' daily life.

As far as we know, it has not been proposed yet an evaluation protocol that permits to assess all the components of SA, in the context of the same and familiar ADL tasks. This protocol might be helpful to differentiate among different ISA profiles based on ecological indexes of all the components of SA. This information would subsequently have important clinical implications, as it might help the selection of more fine-grained rehabilitation approaches for each patient.

Moreover, the fact that SA is highly dependent on the assessed task highlights a potential gap in ADL-based online SA evaluation research. Typically, online SA assessment is conducted within the context of instrumental ADL, and some of the standardized tasks proposed are characterized by the need of multitasking and high working memory demands (Arora et al., 2021; Chudoba & Schmitter-Edgecombe, 2020; Schmitter-Edgecombe et al., 2021). However, this strategy prevents that more severe patients can be assessed with these tools, as the probability that they still continue familiar with these tasks is very low. For this reason we propose that an ideal protocol should also include various task types that differ in overall complexity and recent familiarity for two key reasons. Firstly, incorporating diverse tasks, such as BADL and IADL, would permit to assess whether patients might exhibit different ISA patters for complex/less familiar than for simpler/more tasks. Additionally, such a protocol could be useful to broad the assessment of online SA to a wider range of individuals with different cognitive abilities and impairments. In fact, the assessment in the context of more complex tasks could also permit to identify even mild SA impairments, while simpler tasks might help to evaluate SA impairments in patients with severe cognitive deficits whose daily activities mainly consist of BADL and who rarely perform more complex tasks.

Nevertheless, a drawback of prior ADL-based evaluation proposal relies on the fact that they typically requires the assessing of every spontaneous error that participants generate, and as many researchers and clinicians argue, this constitutes a very resource- and time-consuming procedure (Tania Giovannetti et al., 2019). In this dissertation we were motivated to develop ADL-based assessment methods able to simplify the scoring method to quantify error detection and correction measures.

Another aspect that needs more attention is the investigation of the cognitive mechanisms that underlie ISA, with a special interest in EF. Some studies have reported significant associations between EF and ISA, while others have found null associations between these two constructs. These contrasting findings might be due to the fact that impairments in specific executive mechanisms, rather than global EF deficits, could be associated with ISA. A relatively unexplored component of EF that might play a significant role in ISA is *conflict monitoring*. This hypothesis is primarily drawn from the literature based on the conflict monitoring theory (Yeung et al., 2004), which, based on the shared cognitive and neural activity found in response to the two mechanism, account for the link between conflict detection and the detection of errors during the performance (*i.e. emergent awareness*). However, this link has been less studied in the context of ISA. We are aware of only two studies that explored the association between conflict monitoring and ISA that found significant associations between offline measures of ISA and the performance in the Stroop test, supporting the proposed relationship. Nevertheless, we think that, based on the literature revised, a significant association may also be found also between conflict monitoring and emergent awareness. Furthermore, the literature on conflict monitoring suggests that different cognitive and neural mechanisms may be involved in the monitoring and resolution of different types of conflicts (*e.g.* Stroop, Simon, Flanker tasks). Therefore an unexplored question that motivated this dissertation is to further test whether the ability to monitor and solve different types of conflicts is differentially related to emergent awareness.

The neural network involved in performance monitoring and error detection has been largely studied in the context of experimental tasks. This line of research has offered valuable insights into the specific brain regions involved in these processes, highlighting the significant contributions of the medial cerebral areas, parietal cortex, and insula. However, the revision of the behavioural and neuroimaging research about error detection in the context of ADL-based tasks suggests that a part of common neural mechanisms shared by all types of errors, additional different cognitive and neural mechanisms may be involved in the detection of different types of errors. In line with this previous neuroimaging studies, it has been found that different areas responded to visuospatial errors, object substitution and sequence violation error. These ADL errors might involve very different processes including spatial perception, object perception and use, and steps sequencing. Therefore, it may be more evident that different neural mechanisms should be involved in their detection. However, errors like omissions, repetitions of steps, and violations of sequence all point to the breakdown in the same aspect of ADL: the proper sequencing of the necessary steps to complete the task. As far as we know no studies have investigated if the detection of these different types of sequence errors is supported by the same neural network or if a qualitative neural difference might be found for their detection. Interestingly the sequential aspect of ADL also permits to investigate another feature that may affect performance monitoring and error detection: the predictability of actions. Even if the neural bases of predictability have been largely studied in the context of experimental tasks, few studies explored the cerebral networks related to unexpected events in more naturalistic actions or tasks (Schiffer et al., 2014; Schiffer & Schubotz, 2011; Zacks et al., 2011). Particularly, it seems to be still unexplored whether the brain monitors differently ADL steps depending on their predictability. In addition, we wonder whether the monitoring of unpredictable steps may be somehow related to the detection of ADL sequence errors, since repetition and order violation can be mostly considered surprising unexpected events. These questions constitute the final main motivation of the present dissertation.

Based on these motivations, the general aim of the present thesis is to better understand the different cognitive components and subcomponents of SA and its potential alterations after ABI, within the context of ADL.

The specific goals we will further address are: 1) The development of new methods to assess the online components of ISA after ABI within the context of ADL, and their interaction with the offline metacognitive component; 2) To study the potential relationship between specific executive processes, such as conflict monitoring that might be involved in some components of online SA (*i.e.* emergent awareness) and in offline SA in healthy and ABI patients; 3) To study the neural mechanisms underlying performance monitoring and the detection of different types of errors in ADL sequences in healthy participants.

In order achieve these goals we have conducted three studies that we briefly describe below:

In **Study I (Chapter 6)** we will test the validity of one assessment protocol previously developed in our lab (Merchán-Baeza et al., 2020), designed to provide an exhaustive assessment of all the online components of SA typically identified in influential theoretical models that could be impaired after ABI, within the context of familiar ADL. In this study a group of patients with ABI and a group of age and years of education-matched controls performed two novel ADL tasks designed in our laboratory, the Dressing Conflict Task the Breakfast Conflict Task (Ricchetti et al., in press). During the execution of these tasks, several SA indexes were calculated as measures of different online components of SA. The convergent validity of these measures with measures of the same online SA components based on traditional non-ADL neuropsychological tests analysed. External validity was also investigated, comparing the performance of ABI patients and healthy controls on every online SA index derived from both ADL tasks. A final aim of this first study was to further test the potential relationship between different components of online SA and offline SA. In contrast to prior studies, the fact that both traditional measures of offline SA and our new ADL-based protocol to assess online SA ask participants for their SA abilities with the same functional domains (*i.e.* ADL), might constitute an improved method to directly test their relationship.

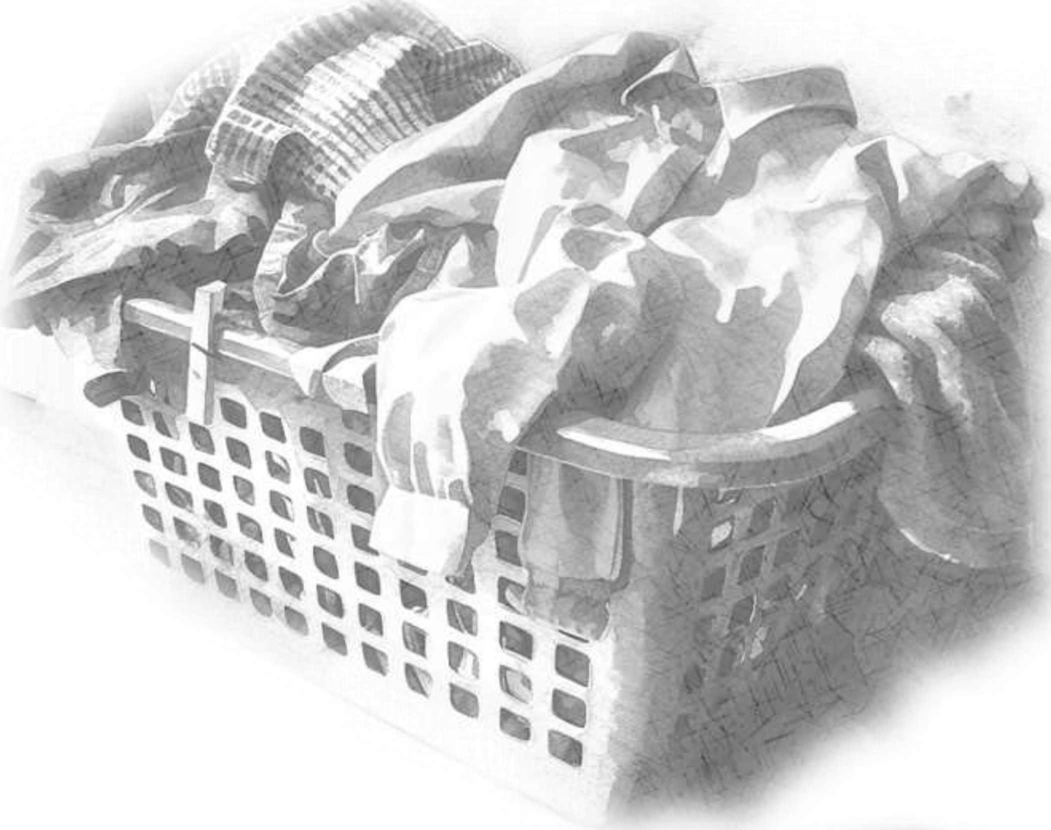
In order to further understand the specific cognitive processes that are implied in SA and could be specifically altered after ABI, we conducted **Study II (Chapter 7)**. Specifically, based on the "conflict detection" theory proposed by Yeung et al. (2004), this second study investigated whether conflict monitoring/resolution is a key EF component related to SA. The first aim of this second study was to investigate whether conflict monitoring/resolution abilities when measured with experimental tasks, are specifically altered in ABI patients with ISA. In addition, we wanted to test whether these conflict monitoring/resolution abilities relates to measures of SA, in particular with emergent awareness and offline SA components, even when these last measures were taken within the context of ADL. To this end, a sample of ABI patients was assigned to the group of severe-ISA or No/Low-ISA based on the discrepancy score of the PCRS (Bivona et al., 2019). Patients with severe-ISA, patients with No/Low-ISA and age and years of education-matched neurologically healthy controls performed an experimental interference task previously designed in our laboratory (Rodríguez Bailón, 2014). This experimental task allowed obtaining a measure of three types of conflicts at a time in an orthogonal manner. The first type of conflict was generated by the presence of distractor stimuli (*i.e.* Visual search requirements), the second conflict type consisted of a stimulus-stimulus conflict (*i.e.* Spatial Stroop interference), and the third conflict type was a stimulus-response conflict (*i.e.* Simon interference). We first explored whether patients with severe-ISA showed impairments in conflict monitoring/resolution abilities when performing the experimental task, compared to the other two groups. Secondly, we analyzed the relationship between the ability to monitor and solve each type of conflict derived from the experimental task and measures of offline SA and online SA measured with functional ADL tests (*i.e.* discrepancy score in the PCRS questionnaire as measure of offline SA and percentage of detected errors in the Breakfast Task validated in Study 1 as measure of online SA).

In Study III (Chapter 8) we focused on the neural mechanisms supporting processes related to emergent awareness in the context of sequence of action in familiar ADL, such as the recognition of different types of sequence errors and the monitoring of different types of steps within the sequence. In this study a sample of young healthy participants observed a sequence of pictures depicting the steps to make a cup of tea. The sequences of steps could be either correct or incorrect if it contained one of the three types of sequence errors described in the introduction (omission, repetition or violation; Chapter 3). One of the specific aims of the present study was to identify the cerebral networks involved in the monitoring of correct and incorrect ADL sequence of steps and in detecting each type of sequence error. In addition, we explored the neural mechanisms related to another aspect of ADL sequences that might affect sequence and errors monitoring, the predictability of next step. To achieve this latter aim each step of the sequence was classified as being more or less predictable based on the probability of being performed depending on the previous step of the sequence (according to normative data derived from a performance-based tea-making task). Cerebral responses on high predictable, low predictable and erroneous steps were compared to understand if these different types of steps are processed by different brain networks.

Finally, the **General Discussion** (**Chapter 9)** provides an integrative view of the results of the three studies that compose the present thesis. Furthermore, the findings derived from the present dissertation will be discussed with special emphasis on three aspects: the potential for improving SA assessment, the implication for enhancing our understanding of the specific cognitive mechanisms that underlie ISA, the possible application for clinical practice. In addition throughout the general discussion we will propose possible new avenues of research that may be explored.

PART III

EMPIRICAL STUDIES



CHAPTER 6

The Breakfast and Dressing Conflict Task

Preliminary evidence of its validity to measure Online Self-awareness after Acquired Brain Injury

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6.1. Abstract

ISA after ABI is a major complication for patients' functionality and independent living. Self-awareness (SA) is described as a construct that is multicomponental in nature, composed of offline SA (*i.e.*, general awareness or metacognitive knowledge) and online SA (*i.e.*, awareness of performance in the context of a given task). Despite the fact that different forms of impaired SA may emerge depending on the affected component, in clinical practice, usually only the offline component is taken into account. In the present study we aimed at providing preliminary evidence of the validity of the *Breakfast and Dressing Conflict Task* to assess online self-awareness in ABI patients and to study its interactions with offline SA. In addition, we tested the validity of a simplified measure of performance monitoring relevant for clinical practice, the ADL-Conflict-Monitoring-Index. To this end, a sample of ABI patients (N=30) and a sample of neurologically healthy controls (N=28) performed two ADL tasks, the Breakfast Task and the Dressing Task among distractors and conflicting situations. The variables emergent awareness, self-regulation, anticipatory awareness and self-evaluation were collected, and their convergent and external validity and their relationship with offline-SA were analysed. The ADL-Conflict-Monitoring-Index was calculated and its convergent validity was tested. Results showed that the online-SA variables of the *Breakfast and Dressing Conflict Task* demonstrated convergent validity with traditional online-SA measures in both tasks. In addition significant differences between groups were found for the emergent awareness and self-evaluation measures from the Breakfast Task and for the self-regulation measure of the Dressing Task.

Significant correlations were found between offline-SA and emergent and anticipatory awareness in the Breakfast Task. The ADL-Conflict-Monitoring-Index proved to be a valid measure for patients' performance monitoring. These preliminary findings suggest that the BD-Conflict-Task is a valid tool to assess online-SA in ABI patients and provide further understanding of the online-offline SA interaction. Furthermore, the ADL-Conflict-Monitoring-Index proposed here may be a valid and easy-to-use monitoring measure in clinical settings.

Keywords: online self-awareness; acquired brain injury; activities of daily living; assessment.

6.2. Introduction

Impaired self-awareness (SA) after acquired brain injury (ABI) is a severe complication that compromises the patient's functional outcomes (Fischer et al., 2004). The Dynamic Comprehensive Model of Awareness (DCMA, Toglia & Kirk, 2000) describes SA as a multicomponent construct. Metacognitive knowledge is the *offline-SA* component that contains almost stable semantic knowledge stored in long-term memory about tasks' characteristics and our abilities to perform them. The *online-SA* component constitutes a group of processes activated during the execution of a given task and is composed of *emergent awareness* (error detection), *self-regulation* (error correction), *anticipatory-awareness* (the ability to predict the incoming task performance) and *self-evaluation* (the appraisal of our performance immediately after the task). One key aspect of the model is the interaction between offline-SA and online-SA through an *updating* process, which consists in the integration of the information derived from our present performance within our prior metacognitive knowledge.

The different components of SA, although interacting with one another, might be independently affected, leading to different forms of ISA. The deficit in emergent awareness is characterized by the failure to detect errors during task execution. This lack of recognition of problems as they arise results in the patient having an inaccurate perception of her/his own abilities and deficits (metacognitive self-knowledge). Several studies support this pattern of impairment, finding that error monitoring abilities during task significantly correlate with offline metacognitive SA (Fitzgerald et al., 2017; Wise et al., 2005; however see Giovannetti et al. 2002; for findings of null association between emergent awareness and offline SA).

On the other side, some patients are able to detect, correct and even accurately evaluate their own performance immediately after finishing the task. However, because of their memory problems, the information about the new experience vanishes soon after finishing the task, preventing the updating of SA. To test that, some studies introduced the assessment of the updating component, measuring patient's self-rating of the performance with a delay of 20/60 minutes after finishing the task. Stewart et al. (2010) found that patients with Alzheimer's disease had altered anticipatory awareness, but SA improved immediately after experience, with the patients showing a more accurate self-evaluation. However, when measuring SA again one hour later, the accuracy of patients SA had returned to pre-task level. The different patterns of impairment described above evidence the need of evaluating all the components of SA, since different rehabilitation strategy should be implemented depending on the process that is affecting patient's ISA.

In line with this, a recent review about the DCMA (Toglia & Goverover, 2022) highlights the importance of developing new assessment tools that enable the evaluation of all the online-SA and updating components. In addition the authors emphasize the need of assessing all the SA components in the context of functional tasks. Most studies have used laboratory tasks or neuropsychological tests to measure online-SA (Chiou et al., 2011; Dockree, Tarleton, et al., 2015; FitzGerald et al., 2012; Fitzgerald et al., 2017; Hergert et al., 2020; Hoerold et al., 2008; O'Keeffe et al., 2007a, 2007b; Plutino et al., 2020; Quiles et al., 2020; Robertson & Schmitter-Edgecombe, 2015; Torres et al., 2016). The lack of patients' previous experience with these artificial tasks, however, might limit its validity to measure online-SA, since performance prediction, monitoring and self-evaluation cannot be based on prior task knowledge and on how they dealt with

similar tasks in the past. Additionally, these tasks may not reflect real online-SA deficits when patients' face familiar and meaningful tasks in their daily living (ADL).
A final concern of using these non-familiar measures on online SA, is that they may not be appropriate to study the potential online-offline SA relationship, since offline-SA is typically assessed with questionnaires about the patient's difficulties with functional activities (Al Banna et al., 2016).

In an attempt to overcome these concerns, some studies have proposed assessment tools of online-SA within the context of ADL tasks (Arora et al., 2021; Bettcher et al., 2008; Chen & Goverover, 2021; Chudoba & Schmitter-Edgecombe, 2020; Doig, Fleming, & Lin, 2017; Doig, Fleming, Ownsworth, et al., 2017; Giovannetti, Libon, & Hart, 2002; Giovannetti et al., 2007; Goverover et al., 2014, 2020; Hart et al., 1998; Jaywant et al., 2022; Rotenberg-Shpigelman et al., 2014; Schmitter-Edgecombe et al., 2021; Seligman et al., 2014; Zlotnik & Toglia, 2018). Nevertheless, to the best of our knowledge, none of them have measured all online-SA components proposed by the DCMA within the same task. For example, the studies from Giovannetti's laboratory focus on error detection and correction abilities during task execution, but do not evaluate anticipatory awareness, self-evaluation and/or updating components (Bettcher et al., 2008; Giovannetti, Libon, & Hart, 2002; Giovannetti et al., 2007; Hart et al., 1998; Seligman et al., 2014). On the other hand, the studies using the Weekly Calendar Planning Activity measured online emergent awareness during the task and/or self-evaluation after the task, while the other components of the online SA and the updating component were not assessed (Arora et al., 2021; Goverover et al., 2020; Jaywant et al., 2022; Zlotnik & Toglia, 2018). Finally, Chudoba & Schmitter-Edgecombe (2020) evaluated anticipatory and self-evaluation SA prior and after task performance, so as the updating component, but the online components of emergent awareness and self-regulation were not assessed. Therefore, an evaluation protocol based on structured observation of well-known ADL that addresses all types of online components of SA at a time is still required.

Another concern present in most of these ADL studies, is that they typically face participants with ADL that are instrumental in nature, requiring multitasking and the interaction with a large number of objects and steps (Chudoba & Schmitter-Edgecombe, 2020; Goverover et al., 2020; Schmitter-Edgecombe et al., 2021). Meanwhile these tasks seem be very sensitive to identify subtle cognitive and SA alterations in patients with mild cognitive problems (*e.g.* MCI, elderly, or mild ABI) they may not be that useful for more severe patients that are not performing these complex task in their daily practice, due to the se severity of their illness, which might be more restricted to more basic ADL (teeth brushing, dressing, etc.).

Finally, an important inherent difficulty of the evaluation of online-SA with performance-based ADL tasks is that emergent awareness and self-regulation are usually measured based on the patient's ability to detect and correct errors that occur spontaneously along the task and that cannot be anticipated by the clinician beforehand. For this reason, patients' performance need to be video-recorded and evaluated offline, codifying all the errors that the patient committed and for each error score whether the patient has detected and successfully corrected it. This approach makes the evaluation highly resource- and time-consuming, preventing its applicability in clinical settings (Giovannetti et al., 2019). Therefore a desirable characteristic of ADL-based assessment tools is to provide an easier and more practical way to score error detection and correction during task performance.

We have recently proposed an ADL evaluation protocol with the aim to address the issues described above (Merchán-Baeza et al., 2020). The designed protocol would permit to assess all the online-SA components within the context of the same ADL. The tool is composed of two ADL tasks (an instrumental ADL [preparing breakfast] and a basic ADL [getting dressed]), both of which include a set of distracting objects and unexpected conflicting situations that must be solved in order to successfully complete the tasks.

First, the introduction of a basic ADL *i.e.* dressing, apart from an instrumental one constitutes a relevant novelty for online SA assessment, as most prior tools are based on the performance of instrumental ADL tasks. The inclusion of a basic ADL in the protocol permits to evaluate online SA in more severe patients that don't have daily experience of that complex ADL in their actual routines. In addition, evaluating online SA in the context of both a basic and an instrumental ADL might permit to better understand the role of task difficulty on online SA, as very few studies have previously study that (Rotenberg-Shpigelman et al., 2014). Second, the introduction in this protocol of distracting objects and conflicting situations might also have several advantages. On the one hand, they might enhance the similarity with real-word situations, increasing ecological validity. More importantly, the presence of distracting and conflicting increases tasks' monitoring demands in a very specific way. This, in turn, may facilitate the assessment of patients with a wide range of abilities and impairments. Indeed, research has shown that elderly participants and individuals with mild cognitive impairment tend to produce very few overt errors (Bettcher & Giovannetti, 2009; Rycroft et al., 2018; Schmitter-Edgecombe et al., 2021; Seligman et al., 2014). However, the introduction of unexpected situations that require resolution during task performance enhances the potential for observing monitoring and self-regulation impairments, even if they are mild (Merchán-Baeza et al., 2020). Finally, the inclusion of distracting objects and conflicting situations will constitute evoked situations where the evaluator can focus on during the assessment of error/conflict detection and correction. If the codification of patient's ability to deal with these distractors and conflicting situations proves to be sufficient to account for emergent awareness and self-regulation abilities, it could be an easy-to-use measure of online SA potentially applicable even to clinical settings, as it won't require codifying other spontaneous errors that might emerge during the task.

The main aim of the present study was to provide preliminary evidence of the validity of this protocol to assess online-SA components and the updating process in ABI patients. To this end we studied the convergent and external validity for each online-SA and updating measure derived from the ADL-based protocol. Secondly, we aimed at testing the interactional nature of the DCMA, by analyzing the relationship of all online-SA components with offline-SA, measured within the same functional domain. The last aim of this study was to test whether the assessment of emergent awareness and self-regulation abilities exclusively based on patients' behavior towards evoked distracting and conflicting situations is suitable to assess online-SA in a simplified manner.

We expected to find convergent validity for the online-SA variables of the proposed protocol with traditional online-SA measures. We also expected to find external validity for the online-SA measures derived from the protocol, with these measures successfully discriminating between ABI patients and neurologically healthy controls. In addition, we expected a pattern of interaction between several online-SA components and offline-SA. Finally we expected emergent awareness and self-regulation to be validly assessed exclusively focusing on the patient's actions towards distractors and conflicting situations.

6.3. Method

6.3.1. Participants

A total of 41 brain injury patients were recruited from Neurological rehabilitation services and ABI associations in the cities of *Granada* and *Málaga*. The eligibility criteria were: age >18 years, diagnosis of ABI and absence of premorbid psychiatric disease. The exclusion criteria were: presence of aphasia, hemineglect, perception deficits, severe motor impairments in both upper limbs and Mini-Mental State Examination<18 (MMSE, Lobo et al., 1999). These criteria led to the exclusion of 5 patients and another 6 patients did not complete the evaluation. Therefore, a final sample of 30 patients (11 females and 19 males; was included in the study. 26 patients had suffered a cerebrovascular accident (19 ischemic and 7 haemorrhagic) and 4 patients had suffered a traumatic brain injury (mean time since injury = 33.4; SD = 54.5). A sample of 28 healthy controls (HC; 21 females and 7 males participated in the study.

The study protocol was registered in ClinicalTrial.gov (NCT03712839) and approved by the Andalusian Ethic Committee for Biomedical Research (AnosognosiaAVD2017, 0056-N-17). Prior to participation, all participants received verbal and written information about the study and gave their written informed consent to participate and to be video-recorded during the evaluation sessions that required that.

6.3.2 Procedure

Socio-demographic (gender, age and years of education) and clinical information (brain damage etiology and time since injury) was collected from all participants.

Measures

Familiarity with the Breakfast and Dressing tasks

The previous familiarity with the protocol's tasks was assessed by asking each participant how often he/she was used to perform each ADL included in our protocol before and after the ABI, where: 1= never, 2= rarely, 3= weekly and 4= every day.

Neuropsychological measures

The Rey Verbal Auditory Learning Test (Rey, 1964) was used as a measure of episodic memory. The sum of the words recalled in the free call immediately after the list presentations (5 trials) was used as a measure of short memory and the number of words recalled in the free recall test after 20 minutes was used as a measure of delayed memory. These two measures were the traditional measures used for the convergent validity analyses of the self-evaluation and updating components respectively.

The Color Trail Test (D'Elia et al., 1996), Key Search (Behavioural Assessment of the Dysexecutive Syndrome; Wilson, Alderman, Burgess, Emslie, & Evans, 1996), the INECO Frontal Screening (IFS) (Torralva et al., 2009) and Controlled Oral Word Association Test (COWAT) FAS Word Fluency and Category Fluency animals (Benton & Hamsher, 1976), were used to evaluate executive functions. Total direct scores were used for Key Search, IFS and verbal fluency tests. For the CTT the measures used were the time difference between part 2 and part 1, the errors and the near-misses in part 2.

A *Cognitive-Index* was calculated as the average of age-adjusted scores of all neuropsychological tests (excluding the measures used for convergent validity analyses).

A *COWAT-Monitoring* index was calculated on the FAS fluency test as the sum of intrusion and perseveration generated/total word generated. Based on prior research, this index was used as traditional measure of emergent awareness (Robertson & Schmitter-Edgecombe, 2015) and included in the convergent validity analyses in the present study.

Measure of Offline self-awareness

The Patient Competency Rating Scale (PCRS, Prigatano, 1996; Prigatano et al., 1998) was administered in order to assess the offline component of SA. The PCRS asks the patients and a significant other (caregiver, familiar, etc.) to rate, in two different forms, the difficulties that the patient faces during their daily activities (accounting for functional, cognitive, interpersonal and emotional aspects). The discrepancy between the total scores of the patient and significant-other forms was calculated and used as index of patient's offline SA. In addition, the mean rating of the significant-other form was used as the patient's *functionality* measure.

Measures of Online-SA: The Breakfast and Dressing Conflict Task (BD-Conflict-Task)

During the performance based ADL-Tasks participants had to complete the following tasks one at a time: 1-Breakfast Task (BT): prepare an orange juice with a teaspoon of sugar and a toast with butter and jelly and 2-Dressing Task (DT): dress up the upper-body to go out in a rainy day. Both tasks were performed with the participant sitting or standing in front of a table with all the target objects necessary to perform the given task on it. Among the target objects, distractor objects were present. These distractor objects were semantically related to the target task (*i.e.* breakfast or dressing) but were not necessary to perform the specific required task (*i.e.* objects to make a cup of coffee with milk or objects needed to dress to go to bed). As distractors we decided to use items that constituted the whole object set necessary to complete a semantically related non-target task (i.e. all objects to prepare instant coffee among objects to prepare the target tasks of toast and orange juice), as prior work from our lab has shown that MCI and dementia patients were particularly prone to produce tangential actions towards this kind of contextually related distractors (Rodríguez-Bailón et al., 2017). In addition, the tasks presented conflicting situations that the participant had to solve in order to successfully complete the task. In Table 6.1 are depicted the target and the distractor objects and the conflicting situation of each task and Figure 6.1 displays pictures that illustrate the arrangement of the table and the box during the Breakfast and Dressing tasks, as well as the conflicting situations and distracting objects in both tasks.

Table 6.1. Description of the target and distractors objects and conflicting situations used in the Breakfast and Dressing Conflict Task.

Orange juice with a teaspoon of sugar and one toast with butter and jelly		
Target objects	Distractor objects	Conflicting situations
• Four half oranges on a plate • Juice maker • 1 glass • 2 teaspoons • Sugar • Toaster • Bread • Butter • Jelly • 1 knife • 1 additional plate	• Milk • 1 cup • Coffee	• Juicer disassembled • Juicer unplugged • Toaster unplugged • The knife needed to spear the butter was placed inside the jelly jar
Dressing the upper body to go out in a rainy day		
Target objects	Distractor objects	Conflicting situations
• A shirt • A raincoat	• A pyjama (shirt and trousers) • A housecoat • A pair of socks	• Shirt sleeves turned inside out • Raincoat sleeves turned inside out • A clothespin hanging from the shirt collar • A sock hanging from the raincoat pocket.

Figure 6.1 Pictures on the left hand side depict one example of table presentation for the Breakfast Task (top), with the respective conflicting situations and distractors object (bottom). Pictures on the right hand side depict the basket presentation used for the Dressing Task (top), with the respective conflicting situations and distractors objects (bottom).

The detailed procedure of the ADL-based evaluation protocol is described in (Merchán-Baeza et al. (2020). Firstly the evaluator asked the participant to name all the objects placed on the table or in the basket. Secondly the exact instructions for the task were given to the participant. After the instructions were given, the participant was asked to repeat them to ensure their understanding and codification. If the participant did not correctly repeat the requested tasks, he/she was asked again until the instructions were correctly repeated.

The performance on these two tasks was video recorded and posteriorly assessed by two independent raters using a sophisticate classification (based on Bettcher et al., 2008) that relies on the ability of patients of detecting and correcting errors and/or conflicting situations while performing the task (see next section for a detailed description of this classification). The types of errors taken into account during the assessment were based on previous studies about error in naturalistic tasks (R. P. Cooper et al., 2005; Giovannetti, Libon, Buxbaum, et al., 2002; Schwartz et al., 2002a). See Table 6.2 for a brief description of the types of errors assessed.

Table 6.2. Description of the type of errors assessed during the activity of daily living tasks.

Type of errors	Description
Omission	A step needed for the task is not performed
Sequence	Two or more steps of the task are performed in an illogic order
Visuoconstructive	An object (or its parts) necessary to perform a step of the task is used or arranged in a wrong position
Object substitution	A needed step of the task is performed with the wrong object
Repetition	A step of the task is unnecessarily performed more than once
Perseveration	An action is repeated when it has been already completed
Addictions	A step that is unnecessary for the task is performed
Tangential actions	Actions performed with distractor objects to perform the no-target task

Measures of emergent awareness and self-regulation

Based on previous studies (Bettcher et al., 2008; Giovannetti, Libon, & Hart, 2002; Hart et al., 1998), each error observed during the participant's ADL performance was considered as detected when the participant either 1) verbalizes that there is some problem with the task, 2) attempts to correct an error or 3) efficiently corrects the error in the moment that it occurs or in every moment throughout the performance. Error corrections were differentiated in inefficient attempts of corrections and efficient corrections. Combining detection and correction classifications 4 levels of self-monitoring could be created: 1) Undetected error; 2) Detected error without correction attempt; 3) Detected error with inefficient correction attempt; 4) Detected error with efficient correction. For conflicting situations an additional category was introduced: 5) Anticipated and solved conflicting situation, when the participant recognized and corrected the wrong situation before beginning the action with the involved object. Starting from this classification two variables were calculated in order to study on-line awareness components of emergent awareness and self-regulation.

Emergent awareness: the percentage of detected errors was calculated as the sum of all spontaneous errors that the participant detected (self-monitoring levels 2-4) and detected or anticipated conflicting situation (level 5) / total error (including all conflicting situation).

Self-regulation: the percentage of corrected errors was calculated as the sum of spontaneous errors that was efficiently corrected (self-monitoring level 4) and efficiently corrected (level 4) or anticipated conflicting situation (level 5) / detected errors and detected or anticipated conflicting situations.

An *ADL-Conflict-Monitoring-Index* was calculated for the patient's behavior towards distractors and conflicting situations in the BD-Conflict-Task, taking into account the patient's detection/correction capacity. Each conflicting situation and action with distractors was scored as follow: 0=the participant anticipated the conflicting situation/no use of distractor; 1=the participant detected the conflicting situation/use of distractor and efficiently corrected it; 2=the participant detected the conflicting situation/use of distractor but could not efficiently correct it; 3=the participant did not detect the conflicting situation/use of distractor or detected it but did not try to correct it. The percentage of errors with distractors was calculated as the patient's score of distractors use divided by the total possible score of distractors use. Although the number of conflicting situations was always the same within the task, not all the participants faced them all. Therefore, the percentage of errors with conflicting situations was calculated as the patient's score of conflicting situations divided by the maximum score the patient could obtain based on the number of faced conflicting situations. The ADL-Conflict-Monitoring-Index was the sum of the percentages of errors with distractors and conflicting situations, where greater scores indicate worse conflict/error monitoring.

Anticipatory awareness and self-evaluation

In order to measure anticipatory awareness, for each ADL task, after providing the instructions and before the performance, the participant was asked to estimate their performance on a 5-point Likert-scale ranging from 0 to 4 where 0='I won't be able to do it'; 1='I can do it, but I will make many mistakes'; 2='I can do it, but I will make some mistakes'; 3='I will do it quite well, with few errors'; 4='I will do it perfectly without making any mistakes'. This estimation was then compared with the actual participant's performance. To do so, the participant's total error absolute score was converted to a Likert-scale ranging from 0 to 4: 0='can't do the task'; 1='many errors'; 2='some errors'; 3='few error'; 4='no errors'. This transformation was done calculating the z-scores of the total number of errors for each participant (including ABI patients and healthy controls) and assigning to each range of z-scores a score of the Likert scale: $z \leq -0.5 = 4$ 'no errors'; $-0.5 < z < 0 = 3$ 'few errors'; $0 < z < 0.5 = 2$ 'some errors'; $z > 0.5 = 1$ 'many errors'; if the participant could not complete the task = 0 'can't do the task'). After this transformation, a discrepancy index between the two scores (prediction minus actual performance) was calculated to obtain a measure of anticipatory awareness in an ordinal scale where 4 was the maximum anticipatory overestimation and −4 was the maximum anticipatory underestimation.

To measure self-evaluation, the same 5-point Likert-scale was used immediately after the performance of the task, asking the participant to rate their performance. The items of this post-evaluation Likert-scale were 0='I couldn't do it'; 1='I could do it, but I made many mistakes'; 2='I could do it, but I made some mistakes'; 3='I did it quite well, with few errors'; 4='I did it perfectly without making any mistakes'. This post-estimation was then compared with the actual performance Likert-scale score (calculated based on total errors z-scores as described above). The discrepancy index between the two scores (post-evaluation minus actual performance) was calculated to obtain a measure of self-evaluation in an ordinal scale, where 4 was the maximum self-evaluation overestimation and −4 the maximum self-evaluation under-estimation.

In addition, the participant answered 4 questions during the post-task self-evaluation assessment: 1) If you did some errors, which errors did you make? 2) Have you found some difficulties or problems during the task? Which one/s? 3) If yes, did you manage to solve it/them? 4) What did you have to do? Repeat the instruction of the task, please. These questions were introduced in order to obtain a qualitative self-evaluation measure of task performance.

Updating

Twenty/thirty minutes after the immediate post-evaluation the same Likert-scale was administered to the participant. The update variable was calculated as the difference between the delayed self-evaluation and the immediate self-evaluation. The participant also answered the same 4 questions as in the self-evaluation assessment.

However, the delayed self-evaluation was available only for 15 patients in the BT and 13 patients in the DT, and it showed small variance, since only 4 patients in the Breakfast Task and 3 patients in the Dressing Task changed their self-evaluation after 30 minutes, in relation to the immediate self-evaluation. Therefore, this measure was excluded from the final analyses.

Table 6.1. Online-SA measures of the BD-Conflict-Task and traditional online-SA measures

Measures of the Breakfast and Dressing Conflict Task	Traditional measures
Emergent awareness: percentage of detected errors (sum of all spontaneous errors and conflicting situations detected and/or anticipated by the participant divided by the total error including all conflicting situations). ***Self-regulation*****:** percentage of corrected errors (sum of spontaneous errors and conflicting situations efficiently corrected and/or anticipated by the participant divided by the total detected and/or anticipated errors and conflicting situations).	***COWAT-Monitoring:*** sum of intrusion and perseveration generated divided by total words generated in COWAT-Phonetic (Robertson & Schmitter-Edgecombe, 2015).
Anticipatory awareness**:** difference between patient's estimation of their performance prior to the task and the actual patient's performance, ranging from 4 (maximum anticipatory overestimation) to -4 (maximum anticipatory underestimation).	
Self-evaluation**:** difference between patient's evaluation of their performance immediately after the task and their actual performance, ranging from 4 (maximum self-evaluation overestimation) to -4 (maximum self-evaluation underestimation).	***Short-term memory score:*** sum of the words recalled immediately after list presentations in the Rey Auditory Verbal Learning Test (5 trials).

A total of 29 patients formed the final sample for the BT (one patient was excluded, who, due to cultural background, was not familiar with the task) and 23 patients performed the DT. Few neuropsychological data were missing (8.5%) and were not replaced with any values. Eleven patients missed the COWAT-Monitoring and 4 patients the significant-other PCRS form and thus they were excluded from the corresponding analysis.

6.4. Plan analysis

All analyses were performed with IBM SPSS version 28.0. Inter-rater reliability for error classification was analysed on 20% of the sample (randomly selected) through the intra-class correlation coefficient.

Non-parametric tests were used due to the non-normal distribution of the data. The relationship between the online-SA variables of the BD-Conflict-Task and socio-demographic and clinical variables was analysed with two-tailed Spearman's correlations. Convergent validity for each of the online-SA variables of the BD-Conflict-Task was tested with one-tailed Spearman's correlations. For variables that significantly correlated with demographic or clinical variables, these correlations were repeated controlling for such variables. To study external validity Mann-Whitney between-groups tests were performed for each online-SA measure derived from the BD-Conflict-Task. The online-offline SA relationship was studied with one-tailed Spearman's correlations. Convergent validity of the ADL-Conflict-Monitoring-Index was analyzed with one-tailed correlations with the COWAT-Monitoring.

Alpha was set at 0.05 and Benjamini-Hochberg correction was applied to control for multiple comparisons, since it demonstrates higher power compared to other correction methods (Benjamini & Hochberg, 1995; Olejnik et al., 1997).

6.5. Results

The patients' and HC demographic and neuropsychological information, as well as the patients' clinical information, is reported in Table 6.2. The groups did not differ in terms of age or education. Compared to HC, the patients showed significantly impaired performance in five of the six administered neuropsychological tests.

The raters obtained ICC > .85 in codifying errors as *detected* and *corrected* in both tasks.

Patients' and controls' scores on the BD-Conflict-Task are reported in Table 6.3.

Table 6.2. Patients' and healthy controls' socio-demographical and clinical information

	ABI N=30		**HC N=28**	**F** (*p < .05)
Age	56.7 (12.4)		62 (11.6)	2.8
Years of education	9.7 (3.5)		11.1 (2.9)	2.7
Mini-Mental State Examination	27 (2.3)		28.9 (1)	8.4*
INECO	16.5 (5.4)		22 (4.9)	13.1*
CTT				
Errors	0.7 (0.9)		0.1 (0.4)	7.9*
Near-Misses	0.3 (0.6)		0.2 (0.5)	<1
B-A time (seconds)	95.2 (109.4)		68 (43.2)	2.5
Key-Search	1.3 (1.4)		2 (1.3)	3.1
COWAT				
Phonetic	16 (10.2)		38.6 (15.5)	24.6*
Semantic	12.6 (5.4)		22.7 (9.6)	14*
RVALT				
Short-Term Memory	33.4 (13.4)		47.3 (9.4)	18*
Delayed Memory	5.4 (4.6)		10.6 (2.5)	23.1*
Functionality	3.5 (.8)			
PCRS Discrepancy-Index	20.8 (28.9)			
Familiarity	*After brain injury*	*Before brain injury*		
Breakfast-Task	2.02	2.9	3	
Dressing-Task	4	4	4	

CTT = Color Trail Test; PCRS = Patient's Competency Rating Scale; RVALT = Rey Verbal Auditory Learning Test

Table 6.3. Mean (Range) of patients' and control scores in the BD-Conflict-Task

		ABI (N=29)	HC (N=28)
Breakfast-Task	Total Errors	9.8 (1 - 27)	4.9 (0 - 17)
	Emergent awareness (%)	57.4 (7.1 - 100)	74.4 (18.7 - 100)
	Self-regulation (%)	71.4 (0 - 100)	87.4 (25 - 100)
	Anticipatory awareness	1.1 (-2 - 4)	0.5 (-2 - 4)
	Self-evaluation	1 (-1 - 4)	0.3 (-2 - 4)
	ADL-Conflict-Monitoring-Index	41.2 (5.9 - 119.6)	25.1 (0 - 114.7)
		ABI (N=23)	**HC (N=20)**
Dressing-Task	Total Errors	3.6 (0 - 9)	2.3 (0 - 9)
	Emergent awareness	73.7 (33.3 - 100)	76 (33.3 - 100)
	Self-regulation	81.1 (33.3 - 100)	98.7 (75 - 100)
	Anticipatory awareness	1.1 (0 - 3)	0.8 (-3 - 4)
	Self-evaluation	1 (-1 - 3)	0.8 (-3 - 4)
	ADL-Conflict-Monitoring-Index	34 (0-79.2)	29.9 (0 – 79.2)

Correlations between the BD-Conflict-Task online-SA variables and demographic and clinical variables are reported in Table 6.4. None of the variables were significantly correlated with years of education or functionality, reported by significant-others. Age correlated with emergent awareness, self-regulation and anticipatory awareness in the BT and time since injury with anticipatory-awareness and self-evaluation in the DT. The Cognitive-Index significantly correlated with all online-SA variables in both tasks, except for self-regulation in the DT. Only the correlations involving the Cognitive-Index and the correlation between anticipatory-awareness and time since injury in the DT survived the Benjamini-Hochberg correction.

Table 6.4. Online-SA correlations with sociodemographic, clinical and cognitive variables

		Age	Years of Education	Time Since Injury	Functionality	Cognitive-Index
Breakfast Task	Emergent awareness	-.39*	.15	.26	.27	.55**[1]
	Self-regulation	-.42*	.23	-.03	.13	.52**[1]
	Anticipatory awareness	.37*	-.28	.02	-.29	-.60**[1]
	Self-evaluation	.35	-.16	-.16	-.29	-.54**[1]
	ADL-Conflict-Monitoring-Index	.26	-.25	.04	-.33	-.54**[1]
Dressing Task	Emergent awareness	-.27	.36	.17	.28	.81**[1]
	Self-regulation	-.19	.20	.17	-.01	.31
	Anticipatory awareness	.31	-.13	-.54*[1]	.05	-.60**[1]
	Self-evaluation	.37	-.25	-.51*	.02	-.66**[1]
	ADL-Conflict-Monitoring-Index	.24	-.33	-.03	-.08	-.69**[1]

* = p<.05; **=p<.01 (two-tailed); 1= significant after Benjamini-Hochberg correction

Convergent validity

Emergent awareness significantly correlated with the COWAT-Monitoring in both the BT (N=18) *Rho* = -.64, *p* =.002 and the DT (N=14) *Rho* = -.52, *p* = .027. The correlations of self-regulation with the COWAT-Monitoring did not reach significance: BT *Rho* = -.30, *p* =.12; DT *Rho* = -.19, *p* = .26. Self-evaluation significantly correlated with short-term memory in the BT (N=28) *Rho* = -.45, *p* = .008 and DT (N=22) *Rho* = -.69, *p* < .001. All significant correlations survived the Benjamini-Hochberg correction. When controlling for the Cognitive-Index, the correlation between emergent awareness and the COWAT-Monitoring remained significant in the BT *Rho* = -.58, *p* = .007, but not in the DT *Rho* = -.13, *p* = .33. The correlations between self-evaluation and short-term memory were not significant after controlling for the Cognitive-Index, neither in the BT *Rho* = -.03, p = .44 nor in the DT *Rho* = -.35, p = .06.

External validity

The results of the Mann-Whitney analyses derived from the BT showed that the group of patients committed significantly more errors than the HC group U = 600.5, p = .002. Significant differences between groups were also found in on-line SA variables: emergent awareness U = 264, p = .023 and self-evaluation U = 540.5, p = .024. Marginal significant differences were found in the self-regulation U = 294.5, p = .056 and the anticipatory awareness U = 525, p = .050 components and differences were not significant in the Conflict-Monitoring-Index U = 495.5, p = .149.

In the DT patients performed significantly more errors than HC in the DT U = 313.5, p = .038. In relation to on-line SA components a significant difference between groups were found only for the self-regulation component U = 138.5, p = .004. No significant differences were found in emergent awareness U = 217, p = .745, anticipatory awareness U = 271.5, p = .290, self-evaluation U = 246, p = .682 or in the Conflict-Monitoring-Index U = 257.5, p = .498.

Online-offline SA relationship

Regarding the BT (N=26), offline-SA significantly correlated with emergent awareness *Rho* = -.35, p = .038 and anticipatory awareness *Rho* = .47, p = .008. Offline-SA correlation with self-evaluation was marginally significant *Rho* = .33, p = .05, while its correlation with self-regulation was far from significance *Rho* = -.01, p = .47. Offline-

SA correlation with anticipatory-awareness was the only correlation that survived the Benjamini-Hochberg correction. None of the correlations between offline-SA and online-SA components in the DT (N=19) reached significance (emergent awareness *Rho* = -.28, *p* = .24; self-regulation *Rho* = .09, *p* = .72; anticipatory awareness *Rho* = .18, *p* = .45; self-evaluation *Rho* = .15, *p* = .53).

The ADL-Conflict-Monitoring-Index

The ADL-Conflict-Monitoring-Index was significantly correlated with the COWAT-Monitoring in both tasks: BT *Rho* = .65, *p* =.002; DT *Rho*=.57, *p*=.016. After controlling for the Cognitive-Index, the correlation maintained its significance in the BT, *Rho* = .59, *p* = .007, but not in the DT, *Rho* = .19, *p* = .269.

6.6. Discussion

The main aim of the present study was to provide preliminary evidence of the validity of an evaluation protocol based on ADL performance to assess online-SA in ABI patients. To this end, the patients performed the Breakfast and Dressing Conflict Task and measures of online-SA were analysed.

The patients were familiar with the BT and the DT, favouring the general applicability of the protocol used in this study. The online-SA variables in the two tasks did not show significant correlations with years of education, indicating that the protocol may be a valid tool to assess online-SA in ABI regardless of the patients' education level. This result is congruent with previous studies that showed that ADL-based assessment tools are less affected by education variables than neuropsychological tests (Diehl et al., 2005; Manly et al., 1998).

Moderate significant correlations were found between online-SA and age in the BT, which is in line with previous studies that identified age as affecting some online-SA components in complex functional tasks (Arora et al., 2021). Time since injury strongly correlated with anticipatory-awareness and self-evaluation in the DT, favouring the idea that task practice improves online-SA (Doig, Fleming, Ownsworth, et al., 2017; Goverover et al., 2014). In fact, getting dressed is one of the first ADL typically trained during the rehabilitation process, and patients that had more practice with the task after the ABI onset might be more aware of their abilities/difficulties, showing more accurate performance prediction and evaluation. The lack of significant correlations between online-SA and functionality is at odds with previous studies that describe SA as being related to functionality (Goverover, 2004; Villalobos, Caperos, et al., 2020). However, these studies also reveal that the relationship between SA and functionality is highly influenced by other cognitive factors. Indeed, online-SA variables strongly correlated with the Cognitive-Index (including executive and memory functions), which is fully congruent with previous studies that report executive and memory associations with online-SA in ABI patients (Bivona et al., 2008; Ciurli et al., 2010; Goverover, 2004; O'Keeffe et al., 2007b; Zimmermann et al., 2017). Future research is necessary to elucidate the potential relationship between cognitive factors, functionality, and online-SA measured with the present ADL tasks.

Convergent validity

Importantly, the online-SA measures derived from the BD-Conflict-Task showed convergent validity with traditional measures assessing the corresponding online-SA components. As predicted, emergent awareness strongly correlated with the COWAT-Monitoring in both tasks, indicating that these indexes are valid to measure performance monitoring processes within the context of familiar ADL. However, self-regulation measures did not significantly correlate with the COWAT-Monitoring for any of the tasks. This dissociation is in line with the DCMA, which indicates that emergent awareness and self-regulation are two different subcomponents within online-SA. The correlation of emergent awareness with the COWAT-Monitoring maintained its significance even after controlling for the Cognitive-Index in the BT, which shows that the emergent awareness index of this task, despite its strong correlation with other cognitive processes, constitutes a measure of a genuine monitoring process that can be specifically altered after ABI. The fact that the convergent validity of emergent awareness disappeared for the DT when controlling for the Cognitive-Index may indicate that, while error detection relies on more specific monitoring processes in complex instrumental tasks, in easier basic tasks such as dressing, error detection seems to be largely mediated by other cognitive deficits. Self-evaluation strongly correlated with short-term memory in both tasks, which is highly congruent with our predictions. However, these correlations disappeared when controlling for the Cognitive-Index in both tasks. These results are in agreement with the DCMA, for which self-evaluation is the immediate evaluation of the performance, although it also involves other cognitive processes, such as the comparison of the actual performance with the expected performance, its integration with previous knowledge and a self-reflection to understand the consequences of performance difficulties.

External validity

In both tasks ABI patients performed significantly more errors than HC. Previous studies have found that functional impairments in ABI are more evident in IADL than in BADL. Previous studies have found that functional impairments in ABI are more evident in IADL than in BADL (Bottari et al., 2017; De Luca et al., 2018; Farmer & Eakman, 1995)(REF). The fact that in the present study we found significant worse performance also in a basic ADL might constitute novel evidence and may be caused by the presence of the conflicting and distracting situations that, as previously stated, might had increased the monitoring demands of the task. Regarding measures of online SA, ABI patients showed significant poorer emergent awareness and self-evaluation than HC, but this effect was significant only for the BT. This finding is congruent with previous studies (and the DCMA) that found that error detection abilities vary depending on the task performed, with ABI patients showing better online SA in BADL than in IADL (Abreu et al., 2001; Rotenberg-Shpigelman et al., 2014). On the contrary, ABI patients showed lowest self-regulation than HC in the DT, while this difference was only marginally significant in the BT. This finding again supports the idea that emergent awareness and self-regulation are different subcomponent of online SA and that might show different pattern of alteration depending on the task.

No significant differences were found between ABI and HC groups in anticipatory-awareness (only marginal in the BT). These results may be caused by the presence of the conflicting situations in the tasks. Indeed, these situations add monitoring demands to the tasks and the participants had to face unexpected problems during the performance and this might have influenced their prediction abilities about their task performance to both healthy and patient participants. The presence of conflicting situations and distractors might have also affected task performance and emergent awareness and self-regulation components in both groups as reflected by the lack of significant difference between groups in the Conflict-Monitoring-Index. This is congruent with previous studies that demonstrate that in tasks with increased cognitive and/or perceptual demands also healthy participants show not only a worst performance (Botvinick & Bylsma, 2006; Forde & Humphreys, 2000; Giovannetti et al., 2007) but also worst monitoring abilities (Morady & Humphreys, 2009).

The fact that several measures derived from the Breakfast and Dressing Conflict Task did not distinguish between ABI patients and HC may be due to the inherent problem to study external validity in such a complex construct. The ABI group could include patients with different levels of SA, with some patients having preserved SA and other showing severe ISA. In addition it is possible that, given the multicomponential nature of SA, some patients showed specific deficit in some of the components of SA but not in others. In addition, a similar variability might be characterizing HC sample, with some participant showing mild awareness impairment during the task, especially due to the presence of the distractors and conflicting situations. Future study should provide normative data for each measure derived from the present protocol and test whether they can discriminate between patients with and without impairment in each online SA component.

Online-Offline SA relationship

The proposed protocol also allowed testing, in a more direct manner, whether and which online-SA components are related to offline-SA, with multiple measures being taken within the same functional domains and within the same individuals. In the BT, a significant correlation emerged between emergent awareness and offline-SA. This finding is congruent with the DCMA, which affirms that there is a dynamic interaction between these components, since, based on our experiences with specific tasks, we create and/or change our beliefs about our abilities to perform that task. Therefore, patients that show poor performance monitoring may not integrate an appropriate reflection of their current abilities into previous metacognitive knowledge. A significant positive correlation was also found between anticipatory-awareness and offline-SA. This correlation is also congruent with the DCMA. Anticipatory-awareness allows predicting our performance on a specific task based on the information we have in metacognitive knowledge (Toglia & Kirk, 2000). Therefore, anticipatory-awareness strictly depends on offline-SA, and patients that underestimate their deficits "offline" may also underestimate the difficulties they will face when performing a given task. These results constitute an important advance in the study of the relationship among the different components of SA, which had led to controversial findings in the literature described above. The contrasting findings reported in previous research might be due to the different nature of the measures used to assess the different components of SA. In fact in some studies the measures used to assess the offline and the online SA components focused on similar aspects of SA while in other studies the two components were assessed on different domains. For example, Goverover et al. (2014), which did find no relationship between anticipatory awareness and self-evaluation and offline SA, used the self-other discrepancy in the Functional Behavior Profile, a questionnaire that evaluate patient's abilities in performing unspecific tasks and that focus on problem solving and social interaction domains, as a measure of offline-SA. Offline SA measured with this questionnaire is then analysed in relation to the online SA components which were measured by asking for aspects such as the patient's difficulties and the time needed to complete a specific task of internet purchase. In contrast, Rotenberg-Shpigelman et al. (2014) found significant relationship between self-evaluation and self-regulation and offline SA. In this case, the offline SA measure was based on aspects of ISA such as the patient's reactions to experiential and external feedback about the performance and the online SA measures assessed the same aspects of ISA. For example, the self-regulation measure was obtain evaluating if the patient adjusted their self-evaluation after receiving external feedback about performance. The results of these studies support the view of the domain-specific aspect of SA and a resulting conclusion is that careful consideration should be given to the selection of the measures used to assess each component of SA, since they should evaluate similar aspects of SA. The present study might propose ideal conditions in order to investigate the offline-online SA interaction, since the different component measures share the evaluation of functional and cognitive aspects of patient's SA.

In line with this argument, no significant online-offline SA correlations were found in the basic DT. A possible explanation for the lack of significant results in the DT might be that the questionnaire used in the present study (*i.e.*, PCRS) assesses offline-SA by asking about patient's abilities involved to a greater extent in instrumental ADL. Furthermore, as is proposed by the DCMA, SA might change depending on the task performed, and different factors may affect the online-offline SA relationship in basic and instrumental ADL (Toglia & Goverover, 2022). We have recently validated a new scale in our laboratory, “The Cognitive Awareness Scale for Basic and Instrumental Activities of Daily Living” (Salazar-Frías et al., in press), that permits to evaluate the offline SA component based on the discrepancy between the patient and caregiver’s versions, separately for basic and instrumental ADL in ABI patients. The results, showed that meanwhile offline SA measured within the context of IADL significantly correlated with the offline SA measured with the PCRS, the offline SA measured within the context of BADL did not. This finding, again is in line with the domain-specific nature of SA, and highlights the importance of designing and administering tools that evaluate SA in the context of different types of ADL, and this should be applied to both, online and offline SA assessment. As we proposed in Merchan-Baeza et al., (2020), one more straight forward strategy to study the relationship between online and offline SA will be to compare participants’ performance on the present ADL tasks and discrepancy indexes derived from the scale described above. We are presently working to complete this study.

The ADL-Conflict-Monitoring-Index

We also tested the ADL-Conflict-Monitoring-Index, which is a new simplified index of online-SA. This index showed the same convergent validity with the COWAT-Monitoring as the most extensive assessment of patient’s detection of spontaneous errors. Importantly, the assessment of this index is much simpler during task execution, since the assessor’s attention needs to focus on a closed number of patient’s behaviors that can be anticipated. For this reason, this index could be a valuable and easy-to-use measure of performance monitoring in clinical practice.

It is worth noting that this index could not successfully distinguish between ABI patients and HC. However as stated above sample characteristics could have affected this finding. Future studies should test whether this index may discriminate patients with emergent awareness and self-regulation impairments from patients that have these processes preserved. In addition, it would be worthwhile to explore whether this index might be a valuable measure to detect emergent awareness and self-regulation decline also in healthy people.

Limitations

The present study has several limitations. Firstly, due to the situation created by the COVID-19 pandemic, we could not recruit the planned sample and administer all the proposed tests described in the published protocol (Merchán-Baeza et al., 2020). Consequently, our small sample size diminished the power to detect small effects, preventing the generalization of the findings. Nevertheless, an a posteriori sensitivity analysis with G*Power (Faul et al., 2007) showed that our smallest samples (those regarding the convergent validity with the COWAT-Monitoring) were sufficient to detect moderate effects of r = .40 in the BT (N = 18) and r = .46 in the DT (N = 14), with α = 0.5 and 1- β = .80. Furthermore, we could test the a priori established hypothesis, enhancing the statistical power of the analyses. However, further studies are required to confirm the reliability and generalizability of the present preliminary results.

The limited sample size also prevents the possibility to more directly study the potential differences between the online SA measures derived from the BADL *vs.* IADL. The potential differences between the two tasks are suggested by the fact that the measures of online SA in each task showed different pattern of associations with sociodemographical, clinical and neuropsychological variables and with the offline SA components and different pattern of between-groups differences. Nevertheless, further studies are needed to confirm that the present protocol may validly detect if the patient present different level of SA impairments depending on the task assessed.

In addition, the fact that the updating measure showed little variance in both tasks, and that it was only available for few patients, limited the possibility to study it in the present work. In line with this explanation, some studies in metamemory research show that after 1 hour delay patients with neurodegenerative disease significantly changed the evaluation about their performance in a memory test (Stewart et al. 2010). However not such a clear change was encountered when using a 20 minutes delay (Ansell & Bucks, 2006). Future studies including a larger sample and a longer time span between immediate and delayed self-evaluation (*i.e.*, 1 hour) might be more sensitive to isolate specific alterations in delayed self-evaluation (Stewart et al., 2010).

6.7. Conclusions

The present study provides preliminary evidence of the validity of an evaluation protocol to assess all the online-SA components in ABI patients in the context of the same ADL. In addition, empirical evidence that supports the DCMA is provided, enhancing the understanding of the interaction pattern between online-SA and offline-

SA. In addition, we propose a new valid simplified measure (*i.e.*, the ADL-Conflict-Monitoring-Index) to assess performance monitoring that can be easily used in clinical practice (where usually only offline-SA is evaluated) by occupational therapists and other health professionals.

6.8. Acknowledgments

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CHAPTER 7

Identifying Conflict Monitoring as a Key Executive Component Related to Impaired Self-Awareness.

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7.1. Abstract

Impaired self-awareness (ISA) after acquired brain injury (ABI) has been traditionally linked to deficits in executive functions. However, contrasting findings are reported about this relationship probably due to the multicomponent nature of both constructs and the difficulty of traditional measures (*i.e.*, neuropsychological tests) to isolate specific executive components. This study explored whether ISA relates to a less studied executive component, conflict monitoring/resolution. We compared performance of ABI patients with Severe-ISA with performance of patients with No/Low-ISA and healthy controls on the Three-Conflict Cognitive Control Task (3CCT), an experimental task that allowed to obtain three different conflicts indexes at a time (Distractors-filtering, Spatial Stroop and Simon). In addition, we explored the relationship between these conflict indexes with naturalistic online and questionnaire-based offline measures of self-awareness. Patients with Severe-ISA showed impaired conflict monitoring/resolution compared to patients with No/Low-ISA and healthy controls in the 3CCT. Distractor-filtering and Simon conflicts were significantly associated with and predicted both measures of self-awareness. Conflict monitoring/resolution seems to be a key component of self-awareness and should be considered when designing assessment and intervention strategies to deal with ISA.

Keywords:

Self-awareness; executive functions; conflict monitoring; brain injury; naturalistic tasks.

7.2. Introduction

Self-awareness (SA) is an important process required for goal-directed behavior in daily living. The knowledge and experience about one's own strengths and weaknesses is crucial to set realistic goals and adapt actions to different environments and situations. After suffering acquired brain injury (ABI), some patients may present reduced SA of cognitive deficits, which constitutes a severe complication for patients´ functionality and recovery (Dromer et al., 2021b; Fischer et al., 2004; Fleming & Strong, 1999; Hartman-Maeir et al., 2003a; Somon et al., 2017). In the last decade, research has been focused on better understanding which factors predict reduced SA and the cognitive components that may underlie this complex construct (see Brown et al., 2021; Dromer et al., 2021b, 2021a for recent reviews).

Several theoretical models of SA have been proposed, and a common aspect among them is its multicomponent nature (Crosson et al., 1989; Flavell, 1979; Nelson & Narens, 1990; Toglia & Kirk, 2000). A main component highlighted by most models of SA is intellectual awareness or metacognitive knowledge, which is considered "offline" in nature, containing general semantic knowledge about the characteristics of the tasks and our abilities to perform them (Crosson et al., 1989; Toglia & Kirk, 2000). The offline component would be continuously updated based on our daily experiences with the environment, which constitutes the "online" component of self-awareness. This online component would be activated whenever we perform a given task, and it is composed of processes such as monitoring (*i.e.*, error detection) and self-regulation (*i.e.*, error correction), which allow us to be aware of our difficulties in a moment-by-moment manner and to adapt our performance whenever necessary (Toglia & Kirk, 2000). In research and clinical settings, the most frequent assessment tools used to measure the offline component of SA are structured questionnaires, asking patients and their main caregivers about the patient abilities when performing daily activities. Greater discrepancies between the two versions, with the patient overestimating their abilities in relation to the informant rating, are considered indexes of greater impairments in patient's metacognitive knowledge. Online SA, by contrast, is usually studied by measuring participants' abilities of detecting and correcting errors while performing experimental or naturalistic tasks (Al Banna et al., 2016; Dockree, Connell, et al., 2015; Dockree, Tarleton, et al., 2015; Giovannetti, Libon, & Hart, 2002; Hart et al., 1998; O'Keeffe et al., 2007a; Toglia & Goverover, 2022).

Among the cognitive factors, Executive Functions (EF) have been the most frequently studied in association with SA. The interest to study the link between SA and EF might come from models of EF including some forms of metacognition and monitoring as part of their definition (Fernandez-Duque et al., 2000; Kennedy & Coelho, 2005; Miyake et al., 2000; Stuss, 2011). At the empirical level, most studies have found evidence favoring such relationship (Bettcher et al., 2008; Bivona et al., 2008; Bogod et al., 2003; Chen & Goverover, 2021; Coben et al., 1995; Hart et al., 2005; Kashiwa et al., 2005; Noé et al., 2005; Villalobos et al., 2021) (Arora et al., 2021; Zlotnik & Toglia, 2018). However, other studies have found null associations between the performance in EF tests and measures of SA (Bach & David, 2006; Belchev et al., 2017; Chiou et al., 2011; Giovannetti, Libon, & Hart, 2002). These contrasting findings might be due to several reasons. On the one hand, neither EF nor SA are unitary processes, and it is possible that not all aspects of EF are equally relevant for all SA components. Meanwhile the majority of studies have focused on the relationship between EF and the offline component of SA, very few have included measures of online SA. In addition, the tools used to measure EF in most studies were neuropsychological tests (*i.e.*, the WCST, Trail Making test and verbal fluency tests, among others) that might sum the influence of several EF components (*i.e.*, monitoring, flexibility, inhibitory control, self-regulation…). Finally, studies differ in the type of tests used, which prevent direct comparisons across them. Therefore, it is still unknown which component(s) of SA is/are specifically related to which component(s) of EF (Dromer et al., 2021b).

One answer to this question might come from the use of experimental tasks specifically designed to dissociate among different EF in a more fine-grained fashion. Only a few studies have used experimental go-no-go tasks to measure sustained attention and inhibitory EF processes in relation to offline and online SA, finding a positive relationship among them, both in brain injury patients and healthy controls (Dockree, Tarleton, et al., 2015; Harty et al., 2013; Hoerold et al., 2008; McAvinue et al., 2005; O'Keeffe et al., 2007a).

Another candidate component of EF that has received almost no attention about its potential link with SA is *conflict monitoring*. Conflict monitoring is typically measured with Stroop-like experimental interference tasks, where a conflicting situation may arise from different stimuli and/or response dimensions. The typical effect found in interference tasks is that the presence of conflict (*i.e.*, incongruent conditions) leads to a decline of performance (decrease in accuracy and slower response times) compared to non-conflicting situations (*i.e.*, congruent conditions) (Ridderinkhof et al., 2011). Simon, Flankers and Spatial Stroop tasks are among the traditional paradigms used to measure conflict interference effects (Kornblum et al., 1990; Kornblum & Lee, 1995). Whether these different conflict tasks tap into the same monitoring mechanism or whether they depend on separate ones is still a matter of a large debate (Braem et al., 2019; Egner, 2008). Nevertheless, based on one of the most influential theories explaining conflict effects, *i.e.*, the conflict monitoring hypothesis (Botvinick et al., 2001), there is a specific system in the human brain that detects the presence of conflict during information processing and response selection. Interestingly, this theory accounts for the involvement of the same conflict monitoring process during error detection, which is a main component of SA. The model describes conflict and error monitoring as based on the detection of response conflict, prior to response selection for conflict monitoring and posterior to response selection for error monitoring (Nick Yeung et al., 2004). In addition, regarding the neural substrate of these processes, the fact that the same anterior cingulate cortex activation is found in response to performance errors and conditions where an error is likely to occur (more difficult and conflicting conditions) supports the idea that these two processes may rely on the same cognitive mechanism (Botvinick et al., 2001; Iannaccone et al., 2015; O'Connell et al., 2007; Ridderinkhof et al., 2004; Yeung et al., 2004). Accounting for this parallelism, a strong prediction is that a relationship should be found between measures of SA and measures of conflict monitoring in interference tasks. Surprisingly, as far as we know, only two studies have explored this potential relationship, finding significant positive correlation between reduced offline SA and the amount of errors performed on the Color Stroop test in ABI patients (Bogod et al., 2003) and in patients with Alzheimer disease (Kashiwa et al., 2005). The authors only explored the relationship between the verbal Stroop test and offline SA. However, based on the conflict monitoring theory, high associations with conflict measures should also be found for online SA (*i.e.*, error detection), an aspect that has not been explored to date.

Finally, while one strength of using experimental tasks relies on the possibility to isolate specific cognitive processes, an important challenge in experimental neuropsychological research is to test whether these measures with artificial stimuli are able to translate and predict participants' performance in more significant and naturalistic tasks (Culbreth et al., 2020; Dockree, Tarleton, et al., 2015; Mohamed et al., 2019; Overmeyer et al., 2021; Pinto et al., 2023; Saunders et al., 2022). Therefore, one key unexplored issue is whether conflict monitoring when measured with experimental interference tasks can be associated with online-SA based on the participants' behavior in naturalistic settings.

The general aim of the present study was to investigate the relationship between offline and online SA and conflict monitoring/resolution processes. To this end, a sample of ABI patients with Severe-ISA, a sample of patients with No/Low-ISA and healthy controls were tested with an experimental interference task designed in our laboratory (Rodriguez-Bailón, 2014), that validly measures three types of conflict effects (*i.e.*, Distractor interference, Spatial Stroop and Simon). Firstly, we explored whether patients with Severe-ISA showed specific conflict monitoring/resolution impairments when performing the task compared to No/Low-ISA patients and HC. Secondly, in relation to the main aim of the study, we tested the relationship between the ability to monitor different types of conflicts with the different components of SA.

7.3. Method

Participants

Thirty-three brain injury patients were recruited from hospital neurological rehabilitation services and from brain damage associations from the cities of *Granada* and *Málaga* (Spain). Eligibility criteria were: age > 18 years, diagnosis of ABI and absence of premorbid psychiatric disease. Exclusion criteria were: presence of aphasia, hemineglect or perception deficits and score below 18 in the Mini-Mental State Examination (MMSE, Folstein, Folstein, & McHugh, 1975; Lobo, 1999). These criteria led to the exclusion of 5 patients. Therefore, a final sample of 28 patients participated in the study. However, data from two patients were excluded due to a high rate of commission error in the experimental task (>70%) and a final sample of 26 ABI patients was included in the final analysis. Patients' informants were all close relatives: spouses, parents, sibling and son/daughter.

The healthy control group (HC) was formed by 27 healthy participants who were as close as possible to the patients' sample in terms of age and years of education. Eligibility criteria were: age >18 years and absence of psychiatric and neurological disease or global cognitive decline (Minimental State Examination > 26).

The present study was approved by the Andalusian Ethics Committee for Biomedical Research (AnosognosiaAVD2017, 3/01/2017, 0056-N-17) and was conducted in accordance with the ethical standards of the 1964 Declaration of Helsinki (last update: Seoul, 2008). All participants received verbal and written information about the characteristics of the study and gave their written informed consent to participate in the study.

Procedure

Several socio-demographic variables such as gender, age and years of education were collected for all participants. In addition, for the patients' sample, clinical information related to brain damage etiology and location and time since injury was collected.

Neuropsychological assessment

A battery of standardized neuropsychological tests was administered to all participants to assess EF: the Color trail test part B (CTTB, D'Elia, Satz, Uchiyama, & White, 1994), Phonetic Fluency (FAS) and Category Fluency (animals) (Benton & Hamsher, 1976; Larson & Clayson, 2011) and the INECO Frontal Screening (IFS; Torralva, Roca, Gleichgerrcht, López, & Manes, 2009).

Conflict monitoring and resolution: The Three-Conflicts Cognitive Control Task

Participants performed the "Three-Conflicts Cognitive Control Task" (3CCT; Rodríguez-Bailón, 2014), which is a task developed in our laboratory that allows measuring three types of conflict resolution abilities within the context of the same task. The task was programmed and ran through E-Prime 2.0 (Schneider et al., 2002). The participants sat in front of a computer at a distance of approximately 53 cm. All the stimuli of the task consisted in black arrows on a white background. In the 3CCT, three sources of conflict were orthogonally manipulated: distractor filtering, Stroop conflict and Simon conflict. Figure 7.1a shows the trial procedure, which began with the onset of a fixation point in the middle of the screen for 750 ms. After that, the target stimulus, an arrow pointing upward or downward, appeared in one of the four quadrants of the screen (up-right, up-left, down-right or down-left). The stimulus stayed on the screen for 2000ms or until a response was executed, followed by a 1500 ms inter-trial interval. The participants were instructed to respond to the arrow direction by pressing the "v" or "m" key with the index of the left or right hand, respectively. In case of hemiparesis, the participants responded with the index and middle fingers of the non-paretic hand. The key ("v" or "m") associated with each arrow direction was counterbalanced across participants. An acoustic feedback (a 500 Hz tone for 50 ms) was provided to the participant´s errors.

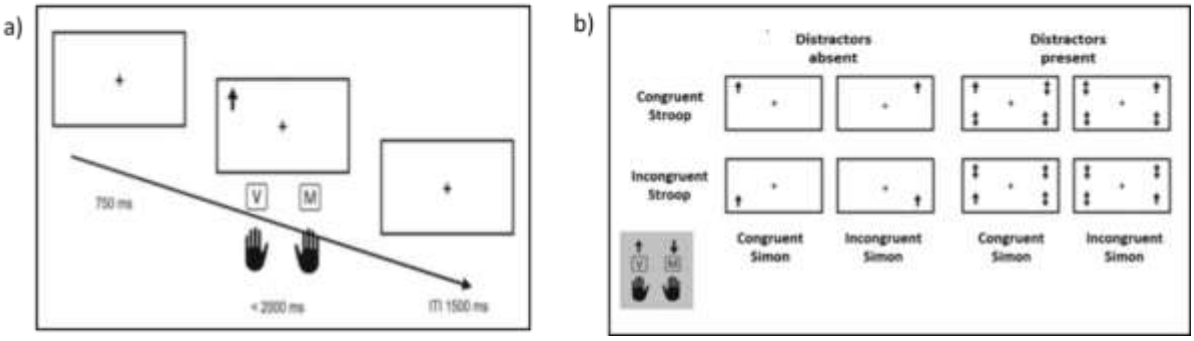

Figure 7.1 Description of the Three-Conflict Cognitive Control Task (3CCT)

Note. Events succession in a trial of the 3CCT (a) and example of the 8 experimental conditions derived from the manipulation of the 3 conflict types in the 3CCT (b). Images adapted from Rodriguez-Bailón (2014).

In 50% of the trials, the target arrow appeared alone in one of the four possible locations on the screen (*i.e.*, Distractors absent condition). In the remaining trials, 3 distracting stimuli, consisting of double-headed arrows appeared simultaneously with the target stimulus occupying the other three possible positions (*i.e.*, Distractors present condition). The spatial position and the direction of the target arrow were manipulated in order to introduce in the task the spatial Stroop Conflict and the Simon Conflict. Stroop congruent trials were those where the target arrow location corresponded to its direction, while incongruent trials were those where the arrow location was opposite to its pointing direction. Finally, Simon conflict arose whenever the irrelevant arrow location was opposite to the location of the correct response.

The three types of conflicts were orthogonally manipulated to ensure that any given trial could be either congruent or incongruent regarding Stroop and Simon conflicts and with or without distractors, leading to 8 different conditions (see Figure 7.1b). All types of trials had the same probability to occur, and were randomly presented within a given block. The task was composed of 8 blocks of 48 trails each. The participants performed the task either in a unique session or in two sessions according to their availability and the level of fatigue.

Self-awareness assessment

Offline SA: Metacognitive knowledge about competency in daily activities

The Patient Competency Rating Scale (PCRS; Prigatano et al., 1998, 1986) is a metacognitive questionnaire that asks the patient and an informant to rate the level of difficulty that the patient experiences when facing daily activities, ranging from 1 (no problem) to 5 (impossible to do). This questionnaire was used to classify patients with Severe-ISA. To assign patients to the Severe-ISA group we applied the double criterion proposed by Bivona et al., (2019): a) patients self-rating score ≥ 100 (indicating minimal self-perceived difficulties) b) positive discrepancy score between patient’s and informant's versions (patient – informant) ≥ 20. The discrepancy score was also used as a measure of offline self-awareness to study its relationship with conflict monitoring processes. The PCRS has demonstrated excellent psychometric characteristics and it has been validated in Spanish speakers (Prigatano et al., 1998).

Online SA: error detection in a performance-based activity of daily living task

The participants completed the "Breakfast and Dressing Conflict Task" (Merchán-Baeza et al., 2020; Ricchetti et al., in press) as part of an evaluation protocol developed in our laboratory to measure online SA within the context of an instrumental activity of daily living. The protocol includes two ADL-based tasks: the Breakfast Task (making an orange juice and a butter and jelly toast) and the Dressing Task (dressing the upper part of the body to go out in a rainy day). We selected the Breakfast Task to measure online SA, since in the previous study (Ricchetti et al., in press) it has demonstrated to validly measure online error monitoring abilities with less influence of general cognitive abilities, compared to the Dressing-Task. The task consisted in preparing an orange juice with a teaspoon of sugar and a butter and jelly toast. The task was performed with the participant sitting or standing in front of a table with all the target objects necessary to perform the given task. Among the target objects, semantically related distractor objects were presented (*i.e.*, objects to make a cup of coffee with milk). In addition, the task presented conflicting situations that the participant had to solve in order to successfully complete the task. The objects' positions were inter-subject randomized through the specific randomization function of Microsoft Excel 2013. The performance was video recorded and subsequently assessed by two independent raters using a sophisticated classification that relies on the ability of patients to detect and correct their own errors and/or to solve conflicting situations while performing the task. The percentage of detected errors was calculated as the sum of all errors and conflicting situations that the participant detected divided by the total amount of errors performed and conflicting situations presented in the task (Merchán-Baeza et al., 2020; Ricchetti et al., in press). This variable was used as a measure of the participants' online SA.

7.4. Plan Analysis

The patient sample was divided into Severe-ISA and No/Low-ISA groups based on the double criterion described above.

One-way ANOVAs were performed to analyze differences between groups in sociodemographic variables, EF tests and SA measures. Regarding the 3CCT, trials with no responses or reaction time < 200 ms were excluded from the analyses. The medians of the reaction times (RT) of the correct responses and accuracy (ACC, percentage of correct responses) were used to calculate conflict indexes for each conflict of the 3CCT (*i.e.* Distractor, spatial Stroop and Simon indexes). RT and ACC conflict indexes were calculated as the average of incongruent condition minus the average of the congruent condition. For RT indexes more positive values indicate higher interference effect while for ACC indexes more positive values indicate lower interference effect. If group differences were encountered on overall RT the analysis would be performed including proportional RT indexes as dependent variable (Hedge et al., 2018). RT and ACC indexes were entered as dependent variables in two mixed repeated measures ANOVAs 3x3 with the type of conflict (Distractor, Spatial Stroop and Simon) as intra-subject factor and group (Severe-ISA, No/Low-ISA and HC) as inter-subject factor. Post-hoc comparison analyses were performed to explore significant main effects and interactions. Second, bilateral one-tailed correlations including all the sample were performed between 3CCT conflict indexes and the percentage of detected errors in the Breakfast-Task and the PCRS discrepancy score. For 3CCT indexes that significantly correlated with age and/or years of education, partial correlations were performed to control for these socio-demographic factors. Finally, in order to further test the contribution made by conflict monitoring measured with the 3CCT on offline and online SA, we conducted multiple regression analyses with the PCRS discrepancy score and the percentage of detected errors in the BT as dependent variables. The independent variables entered in these two regression were the presence of brain injury (group of ABI patients vs. HC) and the conflict index(es) from the 3CCT that, in the previous analysis, significantly correlated with offline and online SA.

The significance level was set at 0.05 and Benjamini-Hochberg correction for multiple comparisons was applied.

7.5. Results

Based on the double criterion of the PCRS scores described above (Bivona et al., 2019), patients were assigned to either the Severe-ISA or No/Low-ISA groups. 2 patients missed the PCRS relative's form and could not be assigned to any group. Consequently, they had to be excluded from any analyses including the group variable. Therefore, 11 patients were assigned to the Severe-ISA group and 13 patients to the No/Low-ISA group.

Some neuropsychological and SA data were missing. The phonetic fluency scores were missing for 2 patients with Severe-ISA, 1 patient with No/Low-ISA and 5 HC, the CTT part B for 2 HC and 1 patient with Severe-ISA. Regarding measures of SA, 5 controls did not perform the Breakfast-Task, and the significant-other form of the PCRS was missing for 16 controls. The missing data were not replaced with any substituted values.

In relation to the 3CCT, 1 patient performed 6 blocks, 5 patients and 6 HC performed 4 blocks and 1 patient performed 3 blocks.

Socio-demographic and neuropsychological data

Table 7.1 shows patients' clinical and lesion information.

As can be seen in table 7.2, the three groups did not significantly differ in age or years of education. Time since injury differed between the groups of patients, with Severe-ISA group showing longer time since injury. Nevertheless, no significant correlation was found between time since injury and online or offline SA measures (Rho=.181, p=.396 and Rho=.277, p=.190 respectively).

Table 7.1 Clinical and lesion information of the patients

ID	Glasgow Coma Scale Score	Etiology	Group	Location of Injury
1	N/A	Ischemic CVA	No/Low-ISA	Right frontal, parietal and temporal; right lenticular and caudate nuclei
2	N/A	Ischemic CVA	No/Low-ISA	Left basal ganglia
3	N/A	Ischemic CVA	No/Low-ISA	Bilateral occipital and left inferior cerebellum
4	N/A	Ischemic CVA	No/Low-ISA	Left hemisphere
5	N/A	Haemorrhagic CVA	No/Low-ISA	Right basal ganglia
6	N/A	Ischemic CVA	No/Low-ISA	Left frontal and parietal and temporal; left lenticular
7	N/A	Haemorrhagic CVA	No/Low-ISA	Left parietal and temporal, left semioval nucleus, left lenticular and corona radiate
8	N/A	Ischemic CVA	No/Low-ISA	Left frontal, parietal and temporal; left semiovale centrum, left frontal white matter, left internal capsule, left basal ganglia.
9	N/A	Haemorrhagic CVA	No/Low-ISA	Left basal ganglia and thalamus, claustrum, corona radiate, left semioval nucleus.
10	N/A	Haemorrhagic CVA	No/Low-ISA	Left basal ganglia and thalamus
11	N/A	Ischemic CVA	No/Low-ISA	Right frontal, parietal and temporal, right basal ganglia
12	4 (severe)	TBI	No/Low-ISA	Right frontal and parietal; Subdural Haemorrhage
13	8/9 (severe/ moderate)	Haemorrhagic CVA	No/Low-ISA	Right frontal, parietal and temporal; internal capsule, right basal ganglia. Subarachnoid Haemorrhage
14	N/A	Ischemic CVA	Severe-ISA	Left frontal
15	4 (severe)	TBI	Severe-ISA	Left mesencephalon; corpus callosum; diffuse axonal

				lesion
16	N/A	Ischemic CVA	Severe-ISA	Bilateral thalamus
17	12 (moderate)	Ischemic CVA	Severe-ISA	Right frontal, parietal (postcentral girus) and temporal; right insula, thalamus and basal ganglia.
18	6 (severe)	Haemorrhagic CVA	Severe-ISA	Cerebellum, left corona radiata, right medial prefrontal and parietal cortex (orbitofrontal and cingulate). Subarachnoid Haemorrhage
19	5 (severe)	Haemorrhagic CVA	Severe-ISA	Left occipital and corpus callosum splenium; posterior left thalamus, cerebellum, left posterior thalamus (pulvinar, geniculate nucleus)
20	14 (mild)	Ischemic CVA	Severe-ISA	Left basal ganglia and thalamus
21	N/A	Ischemic CVA	Severe-ISA	Left frontal and temporal, bilateral parietal
22	13 (mild)	TBI	Severe-ISA	Left frontal and basal ganglia. Subdural Hematoma, Subarachnoid Haemorrhage
23	N/A	Ischemic CVA	Severe-ISA	Right frontal, parietal and temporal; internal capsule, right basal ganglia
24	N/A	Ischemic CVA	Severe-ISA	Right frontal, parietal and temporal; internal capsule, right basal ganglia
25	N/A	Ischemic CVA	N/A	Right frontal and parietal
26	N/A	Ischemic CVA	N/A	N/A

Note. N/A, Not Available; CVA, cerebrovascular accident; TBI, traumatic brain injury

Table 7.2 Sociodemographic, neuropsychological and self-awareness information for acquired brain injury patients with and without impaired self-awareness and healthy controls

	Severe-ISA	**No/Low-ISA**	**HC**	***F*(df)**	***Groups comparisons***
Age	58.5	54.3	58.9	<1 (2,48)	-
Years of Education	9.7	10.8	11.7	1.5 (2,48)	-
Time since injury (months)	41.5 (41.7)	14.3 (15.7)	-	4.8* (1,22)	-
Mini-Mental	27.1	27.6	29.2	6.5* (2,48)	Severe-ISA vs. No/Low-ISA: F<1 Severe-ISA vs. HC: F= 10.2, p=.003* No/Low-ISA vs. HC: F= 12.6, p=.001*
CTT Part B	302.2 (233.3)	203.8 (79.1)	115.9 (49.9)	9.3* (2,45)	Severe-ISA vs. No/Low-ISA: F= 2, p=.169 Severe-ISA vs. HC : F= 14.9, p<.001* No/Low-ISA vs. HC: F= 17.7, p<.001*
Phonetic Fluency	.22.3 (13.4)	18.3 (11)	44.7 (11.8)	23.1* (2,40)	Severe-ISA vs. No/Low-ISA: F<1 Severe-ISA vs. HC : F= 21.1, p<.001* No- ISA vs. HC: F= 40.3, p<.001*
Category Fluency	15.8 (7.4)	14.9 (7.1)	23.9 (8.9)	6.9* (2,48)	Severe-ISA vs. No/Low-ISA: F<1 Severe-ISA vs. HC : F= 6.9, p=.012* No/Low-ISA vs. HC: F= 9.9, p=.003*
IFS	16.3 (6.6)	18.3 (5.3)	23.8 (3.2)	14.1* (2,48)	Severe-ISA vs. No/Low-ISA: F<1 Severe-ISA vs. HC: F= 26.9, p<.001* No/Low-ISA vs. HC : F= 16.6, p<.001*

			Self-Awareness		
% Detected Errors	54 (28.9)	65.4 (25.7)	79.8 (17.1)	5* (2,43)	Severe-ISA vs. No/Low-ISA: F= 1.1, p=.315 Severe-ISA vs. HC: F= 10.5, p=.003* No/Low-ISA vs. HC: F=4, p=.055
PCRS Discrepancy score	48.5 (22.2)	0.46 (10.3)	-1.1 (6.5)	46.5* (2,34)	Severe-ISA vs. No/Low-ISA: F= 48.5,p<.001* Severe-ISA vs. HC: F= 59.2, p<.001* No/Low-ISA vs. HC: F<1

* < .05; CTT: Colour Trail Test; IFS: INECO Frontal Screening; PCRS: Patient's Competency Rating Scale.

Both patients groups, Severe-ISA and No/Low-ISA, showed a significant worse performance in general cognitive screening and neuropsychological tests measuring EF compared to HC but did not differ from one another in these measures. The discrepancy score of the PCRS significantly differed between groups, with Severe-ISA group showing greater offline-SA impairments than both No/Low-ISA patients and HC. No/Low-ISA patients and HC showed similar offline-SA. In relation to online-SA Severe-ISA patients detected significantly fewer errors than HC in the Breakfast-Task. The difference between the two patients' groups in online-SA was not significant and the difference between No/Low-ISA patients and HC was only marginally significant.

Performance on the 3CCT of Severe-ISA, No/Low-ISA and HC

Mean and standard deviation of RT and ACC indexes for Severe-ISA, No/Low-ISA and HC participants are shown in table 7.3.

For RT ANOVA proportional RT indexes were analysed to control for the overall patients' slowing compared to controls (*F*(2,48) = 12.8; *p*<.001; η^2_p = 35). We did so by dividing each participant's RT index by the participant's overall RT mean. The results of the ANOVA on proportional RT showed a main effect of Conflict (*F*(1,50) = 132.3; *p*<.001; η^2_p=.73). Post-hoc comparisons revealed that Distractor conflict (194.9 ms) produced significantly higher interference effect than both Stroop (20.9 ms) (*F*(1,50) = 243.2; *p*<.001; η^2_p=.83) and Simon conflicts (77.6 ms) (*F*(1,50) = 122.6; *p*<.001; η^2_p=.71) and the latter significantly higher interference effect than Stroop conflict (*F*(1,50) = 26.4; *p*<.001; η^2_p=.34). The main effect of Group was significant (*F*(2,49) = 3.5; *p*=.039; η^2_p=.126). Post-hoc comparisons revealed that that the Severe-ISA group (122.3 ms) showed more conflict interference effect than both No/Low-ISA patients (91 ms) (*F*(1,22) = 6.2; *p*=.021; η^2_p=.22) and HC (77.2) (*F*(1,36) = 4.2; *p*=.048; η^2_p=.105). No differences were found between the No/Low-ISA group and HC (*F*(1,38) < 1). The interaction Conflict x Group was not significant (*F*(2,48) = 1.5; *p*=.203; η^2_p=.06). The results of the ANOVA on ACC showed a main effect of Conflict (*F*(1,50) = 7.6; *p*=.002; η^2_p=.12). Post-hoc comparisons revealed that the Simon conflict (-3.1%) produced significantly higher interference effect than Distractor (-0.6%) (*F*(1,50) = 6.2; *p*=.016; η^2_p=.11) and Stroop conflicts (0.2%) (*F*(1,50) = 19; *p*<.001; η^2_p=.28). The difference between Distractor and Stroop indexes were not significant (*F*(1,50) < 1). No significant main effect of Group (*F*(2,49) = 1.8; *p* = .181; η^2_p=.07) or Conflict x Group interaction were found (*F*(2,49) = 1.2; *p* = .325; η^2_p=.05).

Table 7.3 Mean (and Standard Deviation) of RT (in milliseconds) and accuracy (in percentage) of overall 3CCT performance and of each conflict index for Acquired Brain Injury patients and Healthy Controls.

		Severe-ISA N=11	No/Low-ISA N=13	HC N=27
REACTION TIMES (ms)	Overall	1015.8	1052.2	787
	Distractor Index	224.1	202.5	158.2
	Stroop Index	20.3	17	25.4
	Simon Index	122.6	62.4	47.8
% ACCURACY	Overall	91.8	93.6	97.5
	Distractor Index	-2.1	-0.2	0.5
	Stroop Index	1.4	-0.9	0.06
	Simon Index	-4.1	-2.9	-2.2

Relationship between conflict monitoring and online and offline self-awareness

Conflict indexes based on RT, the type of interference measure that clearly discriminate Severe-ISA patients from No/Low-ISA patients and HC, were entered in the correlation analyses. Any RT conflict index correlated with time since injury. The correlations between each RT conflict index and age and years of education showed that the Distractor index significantly correlated with age *Rho*=.328, *p*=.016 and the Simon index significantly correlated with years of education *Rho*=-.316, *p*=.021. No other significant correlations emerged. Therefore, the following correlations concerning the

Distractors index were performed controlling for age and the ones concerning the Simon index controlling for years of education. The correlations between the 3CCT indexes and online and offline SA measures are shown in Table 7.4. The Distractor and Simon Indexes significantly correlated with both detected errors in the Breakfast-Task (online SA) and the PCRS discrepancy score (offline SA). No other significant correlations emerged. All significant correlations survived the Benjamini-Hochberg correction. When repeating the significant correlations only including the ABI patients similar results emerged. Significant correlations emerged between offline-SA and Distractor *Rho*=.505, *p*=.006 and Simon indexes *Rho*=.483, *p*=.010 and between online-SA and Simon index *Rho*=-.430, *p*=.016 and the correlation between online-SA and Distractor index was marginally significant *Rho*=-.296, *p*=.071.

Based on these results we ran two multiple linear regression analyses with the PCRS discrepancy score and the percentage of detected errors in the BT as dependent variables and group (ABI vs. HC), the Distractors Index and the Simon index as predictor variables. The model with the PCRS discrepancy score as dependent variable was significant $F = 11.6$, $p <. 001$ accounting for the 51.2% of the variance and with both conflict indexes emerging as significant predictors Distractor Index $\beta = .291$, $p = .024$ and Simon Index $\beta = .533$, $p < .001$, Group $\beta = .164$, $p = .233$. The model with the % of detected errors as dependent variable significantly accounted for the 35.9 of variance and the Group ($\beta = -.280$, $p = .032$) and both conflict indexes (Distractor Index $\beta = -.319$, $p = .011$ and Simon Index $\beta = -.333$, $p = .012$) emerged as significant predictors.

Table 7.4 Correlations among the experimental indexes of the Three-Conflicts Cognitive Control Task and self-awareness measures.

		PCRS Discrepancy (N=37)	**% of detected errors in the Breakfast-Task (N=48)**
Reaction times Indexes	Distractors Index_RT	*Rho*=.421 *p*=.005*[1]	*Rho*=-348 *p*=.008*[1]
	Stroop Index_RT	*Rho*=.016 *p*=.464	*Rho*=-.085 *p*=.289
	Simon Index_RT	*Rho*=.433 *p*=.004*[1]	*Rho*=-.365 *p*=.006*[1]

Note. * < .05; [1] = significant after Benjamini-Hochberg correction PCRS = Patient Competency Rating Scale.

7.6. Discussion

The main objective of this study was to explore the relationship of online and offline self-awareness with conflict monitoring/resolution processes. To this end, we compared the execution of patients with Severe-ISA after ABI with the execution of a group of patients with No/Low-ISA and that of a group of healthy people in an experimental task that allowed dissociating between the capacity to monitor and solve 3 different types of conflict at a time.

Both groups of patients, showed general cognitive and executive impairments compared to HC. However, the Severe-ISA group and the No/Low-ISA group did not significantly differ from one another in general cognition or executive functions measured with neuropsychological tests. Therefore, we can be confident that the significant differences found between the groups of patients in offline-SA and in the 3CCT task are not due to general cognitive or executive deficits of patients with Severe-ISA. Time since injury was significantly longer for patients in the Severe-ISA group than for patients in the No/low-ISA group. This finding seems at odd with previous studies that state that ISA improves with time (Dromer et al., 2021a). However other studies have found null association between time since injury and ISA (Belchev et al., 2017) or even the opposite pattern with negative correlations between the time passed after the onset of the brain injury and the level of SA (Villalobos et al., 2021). These contrasting findings suggest that time since injury is not directly associated with SA evolution and ISA is a condition that could persist several years after the brain injury, especially without a specific treatment focused on SA rehabilitation (Hart et al., 2009). Importantly, in the present study time since injury did not correlate with SA measures or with conflict monitoring indexes. Therefore, this factor is not affecting the relationship found between SA and conflict monitoring.

In relation to SA measures, the PCRS was the score that clearly distinguished patients with Severe-ISA from patients with No/Low-ISA and HC. Patients with Severe-ISA showed also significant impairments in online-SA compared with HC but not compared with No/Low-ISA patients. This result supports SA models that affirm that online-SA and offline-SA are different components of SA and even if they dynamically interact they can be differentially affected after an ABI.

Interestingly, the results of the 3CCT based on the proportional RT showed that patients with Severe-ISA showed significantly greater conflict interference effect than both HC and patients with No/Low-ISA, suggesting that patients with Severe-ISA have specific impairments in conflict monitoring/resolution. The difficulty in conflict monitoring/resolution was found in RT but not in the ACC. This difference might be due to the different mechanisms that these two measures represent and replicate previous studies using interference tasks that found that RT and ACC measures are not correlated (Kane & Engle, 2003; Prinzmetal et al., 2005).

Importantly, and more related to the main aim of this study, we found a pattern of specific associations between conflict monitoring/resolution processes and SA measures. On the one side, significant correlations were found between Distractor and Simon conflict indexes and the offline measure of SA, the PCRS discrepancy score. The detection and resolution of difficulties during task performance is an important mechanism that could provide metacognitive knowledge about which tasks or task's components are especially challenging and need the recruitment of additional cognitive control or specific strategies (Fernandez-Duque et al., 2000; Shimamura, 2008). Therefore, efficient conflict monitoring and resolution processes might help to be more aware of one's own difficulties and abilities to perform different types of tasks in daily living. However, in line with the dynamic interaction of self-awareness components as stated by Toglia and Kirk (2000), this relationship can be understood in either direction. That is, people with greater metacognitive awareness may better anticipate the cognitive resources and strategies that are needed to efficiently perform the incoming task. Thus, these people may apply more adequate monitoring and control processes during the performance and, as a result, show a lower interference effect in the presence of a conflicting situation.

In addition, the finding that the RT Distractor filtering and Simon indexes derived from the 3CCT were negatively correlated with online-SA when measured as error detection abilities during performance of a daily task is of special relevance since, as far as we know, it has not been previously investigated. This finding empirically supports the existence of a similar mechanism underling conflict monitoring and error detection (Iannaccone et al., 2015; O'Connell et al., 2007; Ridderinkhof et al., 2004; Nick Yeung et al., 2004). However, what is the mechanism shared by error detection and conflict monitoring? Yeung et al. (2004) propose that this mechanism is precisely the one in charge of *conflict detection*. These authors suggest that errors are detected when the activation of the correct response gives rise to a conflict with the previously performed incorrect response and this conflict overpasses a given threshold. In contrast, when the activation of the incorrect response overrides the activation of the correct one, the conflict remains below the threshold, and thus the error is not detected. Similarly, in conflict monitoring/resolution, the activation of the correct response needs to overpass a threshold to be generated and to override the potential incorrect response. Therefore, applying this theory to the results of the present study, those participants that show greater ability (lower RT) in activating and selecting the correct response in the presence of a conflicting situation also showed greater ability to detect errors based on the post-response activation of the correct response.

The correlations with online and offline SA were found only for Distractor and Simon conflict indexes, but not for the Stroop index. A possible explanation for this pattern is that Distractor and Simon conflicts lead to significantly larger interference effects compared to the Stroop conflict during the 3CCT. Longer RT indexes reflect greater conflict, since more time is needed to solve the conflict and execute the correct response. Therefore, if the correlations found in the present study reflect the importance of conflict detection mechanisms for SA, it is possible that the conflict types that generate more interference are the most sensitive ones to investigate the relationship between conflict monitoring and SA. However, another likely explanation could be based on the qualitative difference between the three conflicts types. In Distractor-filtering, Stroop and Simon incongruent conditions the conflict affects different dimensions of the task/stimuli (Frings & Wühr, 2014; Hommel, 2011; Scerrati et al., 2017b). Therefore SA might be especially related with the monitoring of conflicts where the selection of the target stimuli upon distractors and the inhibition of irrelevant but automatic responses are needed.

The present study might also have relevant implications for the renewed emergent interest in determining the ecological validity of laboratory measures (Pinto et al., 2023). In the present study, the conflict monitoring/resolution measures assessed in the laboratory with an artificial and non-realistic task correlated with measures of SA assessed in the context of naturalistic and real everyday tasks. These results add evidence to the argument that certain laboratory measures might be useful to study the cognitive processes involved in everyday activities. In addition, and related to the aim of the present study, the current results give strengthen support to the idea that conflict monitoring/resolution and error detection and metacognition share common cognitive processes. The fact that the Breakfast Conflict Task used in the present study included distractors and conflicting situations, in addition to increasing its degree of similarity with the real world, also increased conflict monitoring/resolution demands. This aspect could have provided the naturalistic and experimental tasks with very similar cognitive demands, facilitating their comparison.

It is important to acknowledge that the sample size of this study was relatively small and caution should be taken about the generalization of the results. However, a posteriori sensitivity analyses with G*Power (Faul et al., 2007) showed that, for the critical correlations analyses, the smallest sample N=37, with α = 0.5 and 1- β = .80 was sufficient to detect small effect size of r = .275. Nevertheless, further research is needed in order to study the reliability of the preliminary results found in the present study. .

7.7. Conclusions

We identified a pattern of association between conflict monitoring mechanisms and online and offline SA in daily tasks. These findings are a valuable source of information that allows progressing in the understanding of how SA works and in delineating the cognitive processes that are important to create and maintain a proper SA. These results also highlight the importance of studying more precisely the specific EF components involved in specific components of SA and the adequacy of experimental tasks to study the potential association amomg them. Conflict monitoring and resolution, given their significant relationship with SA, are among the EF components that should be included in the neuropsychological evaluation and intervention of reduced SA in patients with ABI.

7.8. Acknowledgements

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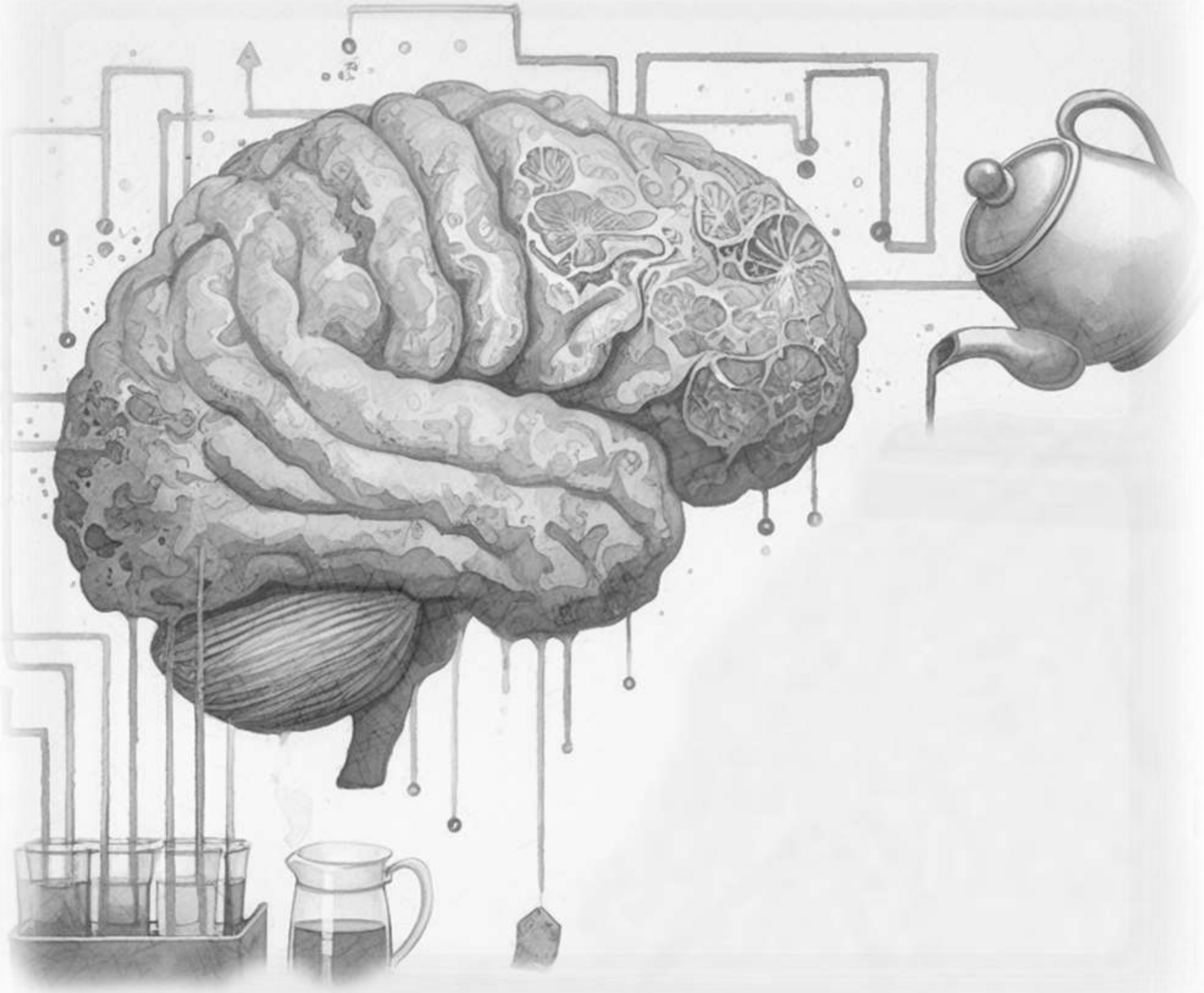


CHAPTER 8

Sequence Knowledge and Step Monitoring in Activities of Daily Living -the Case of Tea Making - an fMRI Study

The content of the present study is in preparation as:

Sequence knowledge and step monitoring in activities of daily living – the case of tea making: an fMRI study.

Giorgia Ricchetti will be the first and corresponding author and Mª Jesús Funes will be a co-author of this work

8.1. Abstract

Sequence knowledge is a nuclear component of activities of daily living (ADL) with sequence errors often result in missing the intended goal. The current study aimed at identifying the neural mechanisms involved in the monitoring of familiar ADL sequence and in the detection of different types of sequence error (*i.e.* omission, repetition and order violation). In addition, we explored the effect of steps predictability in sequence monitoring. Participants were presented with different tea-making sequences that could be either correct or incorrect (including omission, repetition or violation errors) and had to judge their accuracy. Data showed that highly-predictable steps were mainly processed by perceptual and motor areas, partially overlapping with the wider action observation network. In contrast, a network including medial prefrontal and occipital areas, anterior temporal, inferior parietal cortex and the right orbitofrontal cortex processed unexpected actions, including low-predictable and erroneous steps. The left ventral prefrontal cortex specifically responds to sequence errors. Among error types, neural responses are more sensitive to detect the execution of erroneous actions than an omission of step, in line with previous errors models. Additional neural differentiation is found in response to different types of commission errors, with the right superior frontal and middle cingulate cortices responding to violation and left subcortical areas to repetition errors. The present study supports the presence of multiple neural mechanisms involved in monitoring the accuracy of ADL sequences, with different networks monitoring for different sequence events.

Keywords: activities of daily living, sequence knowledge, sequence errors, predictability, functional magnetic resonance imaging

8.2. Introduction

Every day we carry out many activities that are necessary for our functioning and independent living (*e.g.* dressing, driving). These activities of daily living (ADL) rely on interaction with various objects and the execution of multiple steps in a specific order. When the sequence of steps is violated, the task's goal may be compromised. For example, when making a cup of tea, water must be boiled before the tea is brewed; switching the order of these steps leads to failure in the task. In the current study, we aimed to determine the neurocognitive mechanisms that support steps monitoring and error detection in ADL sequences in healthy participants.

An influential model for the execution of ADL proposes a hierarchical tree structure (Botvinick, 2008; Cooper & Shallice, 2000; Cooper et al., 2005; Humphrey & Forde, 1998; Schwartz, 2006). In this structure, top levels describe the generic task goals (*e.g.* make a cup of tea) and branch to the intermediate levels of subgoals (*e.g.* boil water, brew tea), with each further branching to more and more discrete and specific actions (*e.g.* boil water → fill the kettle with water, switch on the kettle; fill the kettle → open the kettle lid, open the water tap…) (Cooper & Shallice, 2000).

When executing an ADL, the process supporting the selection of the next action depends on the location in the hierarchical tree. The selection of actions at the lowest level mainly relies on bottom-up processes based on perceptual affordance and sensorimotor information (*e.g.* a kettle handle affords grasp). Conversely, the selection of actions at the top and intermediate levels relies on top-down processes where the goal and the world state – the presence of preconditions and the previously performed steps – are considered (Cooper & Shallice, 2000; Cooper & Shallice, 2006). Therefore, the correct execution of a sequence depends on executive processes such as working memory, monitoring and inhibition (Forde & Humphreys, 2000; Humphreys & Forde, 1998; Morady & Humphreys, 2009; Niki et al., 2019).

Experimental studies with healthy participants demonstrate that sequence errors increase in high perceptual and cognitive load contexts, like in dual task paradigms, or following distractions or interruptions (Botvinick 2006; Forde & Humphreys, 2000; Giovannetti et al., 2007; Morady & Humphreys, 2009)). Common sequence errors are omissions, repetitions, and order violations (Cazalis et al., 2001; Giovannetti et al., 2007; Hart et al., 1998; Morady & Humphreys, 2009; Reason; 1984) and tend to occur at the subgoal level (R. Cooper & Shallice, 2000; Norman, 1981). Healthy people usually spontaneously recognize sequence errors when they occur, managing to achieve the final goal (Giovannetti et al., 2007; Morady & Humphreys, 2009). The neural correlates of ADL sequence knowledge in healthy participants have been explored using scripts (routine ADL with a specific structure and sequence of events) (Crozier et al., 1999; Knutson et al., 2004; Krueger et al., 2007). In these studies, participants inside the scanner, are presented with action labels, which depict a simple sequence (usually just 2 actions) typically at the top goal level (*e.g.* get dressed/take a shower). These labels appear at the same time on the screen in a determined order (vertically or horizontally arranged) and participants are asked to decide on the correctness of the presented order. The control conditions involve alternative tasks performed with written verbal stimuli, where participants make syntactic (Crozier et al., 1999), semantic (Knutson et al., 2004) or perceptual decisions (Krueger et al., 2007). While studies vary in the specific foci, when taken together, increased responses to the ADL sequence task (versus control tasks) are reported in areas associated with executive function and control in the prefrontal cortices: the inferior and medial frontal, frontal polar and medial superior frontal gyri (supplementary motor area); in areas associated with action and attention control in the superior temporal, inferior parietal cortex; and in high-level visual process in the precuneus and lingual gyrus. Interestingly, many of the reported foci by these studies overlap with areas in the action observation network (Reynaud et al., 2019). However in these studies the neural bases of error detection in ADL sequences were not explored, since the correct and incorrect sequences were collapsed and compared with the non-ADL control condition.

Neural correlates of ADL sequence have also been explored with pictures (Nemmi et al., 2013) and movies (Weiss et al., 2006). Similarly to studies using scripts, those contrasting ADL sequences with non-ADL conditions (*e.g.* navigation route and meaningless manipulations) reported increased responses in the inferior frontal and medial superior frontal gyri, bilateral inferior parietal and superior temporal cortexes extending to the lateral posterior dorsal occipital regions and fusiform gyrus (Nemmi et al., 2013). Besides previous studies, which collapsed correct and incorrect sequences, these studies also explored the neural bases of sequence errors detection. For example Nemmi et al. (2013) analysed separately the neural correlates of correct and incorrect sequences (*i.e.* sequences containing a violation of the steps order). The authors reported that, compared to correct sequences of ADL steps, incorrect ones correlated more strongly with responses of the left middle occipital and fusiform gyri, while the reverse comparison was associated with responses of the right angular gyrus. On the other side, Weiss et al. (2006) compared the neural correlates of different types of ADL errors and reported that, relative to errors associated with the spatial configuration of the action (*e.g.* water being poured next to the glass), errors associated with the violation of the temporal sequence of steps (*e.g.* drinking before the glass is filled) were specifically associated with increased responses in the middle cingulate gyrus (Weiss et al., 2006). Attempts to identify the cerebral areas related to different types of sequence errors are described in the neuropsychological literature (Bailey et al., 2013; Seidel et al., 2013). For example, Bailey et al. (2013) counted the different types of errors made by participants with dementia while performing the NAT (see Table 3.1) and tested the correlations between the frequency of these error types and the volume of different *a priori* selected brain structures. The authors found a qualitative neural differentiation between different error types, and the amount of omission errors negatively correlated with the volume of the medial temporal lobe, meanwhile the production of commission errors (including violation, repetition and object substitution errors) positively correlated with dorsolateral prefrontal cortex (PFC) volume. These studies have relevant implications, confirming the involvement of different cognitive processes in the occurrence of different types of ADL errors. In fact, the study described above supports previous behavioural performance-based based error models (*i.e.* the Omission-Commission model; Giovannetti et al.; 2008) that found that omission errors and commission errors (the performance of a wrong step) correlates with different cognitive domains.

However, in these studies different types of sequence errors (*i.e.* repetition and violation) were collapsed into the same error category (*i.e.* commission errors). In addition, these studies focused on exploring the cerebral areas associated with the production of errors during ADL actual performance, while the neural correlates of error detection were not investigated. Therefore, a still unsolved question is whether, apart from error production, the detection of different types of sequence errors is based on different cognitive processes and neural mechanisms. To the best of our knowledge, no studies have investigated this hypothesis.

An alternative approach to understand ADL sequence monitoring is to consider the predictability of steps. Step predictability is conceptualised using the Markov decision process (MDP) (Puterman, 1990). The MDP is a model used in planning and decision-making problems that makes it possible to calculate the probability value of a given action at a certain point of the sequence taking into account the present state of the environment (*i.e.* the outcomes of the actions previously performed) and both the short and long-term goals (Boutilier et al., 1999). In a given ADL sequence, steps can have different predictable values. For example, in a tea-making sequence, “switch on the kettle” is highly likely to be preceded by “add water to kettle”, and less likely to be preceded by “add teabag to mug” or “add sugar”. The predictability of “add sugar” is weaker than “switch on the kettle”, since it can be performed at any time point of the sequence without affecting the outcome (*e.g.* one can add sugar before or after boiling the water, before or after adding teabag to the mug, etc.). In this context, violation and repetition errors are surprising events as they are unpredictable. The neural correlates of step predictability have been assessed by Zacks et al. (2011). In that study, participants made a two-choice decision about the next step while watching ADL videos (*e.g.* washing a car). The authors reported brain activation in the lateral and medial superior frontal, anterior and posterior temporoparietal and occipital cortex, insula and subcortical basal ganglia when participants made a correct decision about less predictable steps compared to more predictable ones. This study shows how steps predictability is an important aspect that affects the process of selecting the next step when performing an ADL. However whether this aspect also affects ADL sequence monitoring, with different processes and neural circuits involved in the monitoring of highly predictable and low predictable steps, has not been investigated. In addition, as previously stated, taking into account steps predictability, sequence errors such as repetition and violation errors might be considered surprising unexpected events, and therefore, non-predictable events. We wonder whether the detection of sequence errors might somehow be based on the cognitive and neural mechanisms that support the processing of steps predictability.

In the current study, we explored the neural correlates of sequence and steps monitoring of a familiar ADL (*i.e.* making a cup of tea) focusing on different error types and step predictability. We used pictures to depict the steps of tea-making sequences. All the steps pertained to the intermediate level of the sequence hierarchy (*e.g.* “switch on the kettle”, “add teabag to mug”) and were presented as photos from a first-person perspective (Figure 8.1, a). The tea-making sequence could be either correct or incorrect. Incorrect sequences included three types of errors: omission, repetition, or violation. A low-level control condition was included in which the sequences were presented with scrambled versions of the pictures (Figure 8.1, b). The participants’ task was to covertly judge whether a sequence was executed correctly or not. Hypotheses and predictions were made based on previous literature and are fully described above.

In the first analysis, the experimental model considered the entire sequence. Sequences were classified as correct, incorrect (with three error types) and scrambled. The analysis aimed to answer the following questions: 1) what are the neural structures associated with monitoring ADL sequences relative to a low-level visual baseline (*i.e.* scrambled images)? We hypothesized that this generic contrast would reveal widespread activation that would include the action observation network of higher-level visual regions, posterior and middle temporal regions, and motor-associated areas. In addition, we expected to observe activation in areas associated with memory and executive function in frontal regions; 2) what are the neural mechanisms underlying the processing of correct vs. incorrect sequences? We predicted an increased response in the angular gyri in correct sequences and incorrect sequences to be associated with increased responses in the middle occipital, fusiform and middle cingulate gyri; 3) what are the neural structures involved in monitoring different types of sequence errors in familiar ADL? We expected to observe activation in the medial temporal lobe in response to omission errors and in the dorsolateral PFC in response to repetition and violation errors.

In the second analysis, we modelled each event (step) of the sequence. The MDP was applied to normative data of 189 participant performing a tea-making task (involved in a different project, Jean-Baptiste et al., 2016, 2014) and each event was classified into high-predictable, medium-predictable, low-predictable, surprise-unpredictable (*i.e.* errors) and post-erroneous actions. In this analysis, we explored the neural correlates that were sensitive to step predictability. Based on Zacks et al. (2011) study, we expected to find activation in lateral and medial frontal areas, occipital areas and the temporoparietal cortex and basal ganglia in response to less predictable steps and surprise-unpredictable steps (*i.e.* errors) compared to high-predictable ones.

8.3. Method

8.3.1 Participants

All participants were recruited from the University of Birmingham, UK. Twenty healthy participants (17 female/3 male; mean age 24.6 years; 19 right-handed) were recruited to the fMRI study. One participant withdrew from the fMRI study due to claustrophobia, leaving 19 who completed the fMRI session. Thirteen participants completed the post-scanning behavioural task including the participant who withdrew from the fMRI. This behavioural session was conducted to gather behavioural data on sequence knowledge and error monitoring. Participants were either awarded course credits or £15 to compensate for their time.

Twenty-nine different participants (27 females; mean age 20.8 years; 27 right-handed) from the University of Birmingham participated in the second behavioural experiment. In this second experiment the same task used in the fMRI session was used to obtain behavioural data about steps predictability (see below for the detailed description of the task and variables calculation). Three participants were excluded from the analyses since they showed null variability in responses (*i.e.* they responded with the same key press after each step, likely reflecting a misunderstanding of the task). Two additional participants were excluded since they recognized less than 10% of the surprise-error events. Participants received course credits. All participants gave their written consent before their participation. The study was approved by the National Research Ethics Service Committee West Midlands under reference number 12/WM/0220 (27 September 2012) and by the University of Birmingham Ethics Committee under reference number ERN_12-0683B (28 May 2014).

2.2 Stimuli and tasks

The action sequence recognition (ASR) task was run with E-Prime 2.0 software and consisted of the presentation of different tea-making sequences. Each trial began with the presentation of the task goal – the desired tea – for 3000 ms: black tea with sugar, white tea, or white tea with sugar. After that, a white screen with a black fixation point appeared and then the pictures of the tea-making steps (*i.e.* events) were presented one at a time interspersed with fixation point screens. Each fixation point was presented for 300 ms. and each picture was shown for 1000 ms. Trials included 6-8 events (*i.e.* pictures of tea-making steps). Each picture showed a right hand (or a left hand if the participant was left-handed) performing a step of the tea sequence (*i.e.* add water to the kettle) from a first-person perspective (see Figure 8.1 for an example of an ASR task trial). Fifteen different correct sequences (5 for each type of tea) were created based on normative data from 189 participants (ages 18-70 years, all residing in Birmingham, UK) making tea (Jean-Baptiste et al., 2014). Fifteen different incorrect sequences (5 for each type of tea) were created. The incorrect sequences contained an omission, a repetition or a violation error (see Table 8.1 for a description and example of each type of error). For each type of error, five different sequences were created. Three different scrambled sequences (*i.e.* baseline condition) were also included. In the scrambled sequences, the scrambled version of the tea-making steps was presented (see Figure 8.1).

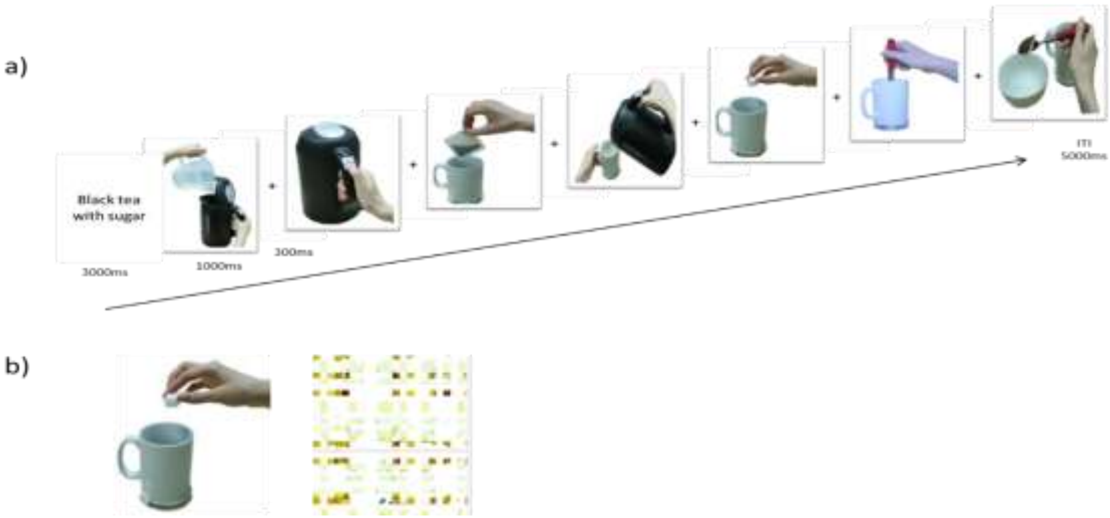


Figure 8.1. (a) Example of a trial in the ASR task depicting a black tea with sugar correct sequence trial that included 7 events. The trial shows “fill the kettle” as the first step (high-predictable), followed by “switch on the kettle” (high-predictable), “add teabag to mug” (high-predictable), “pour water into mug” (medium-predictable), “add sugar” (low-predictable), “stir” (medium-predictable) and “remove teabag” (medium-predictable). (b) Example of a scrambled image vs. its corresponding tea-making action image.

Table 8.1. Example of the types of errors presented in incorrect sequences of the ASR task

TYPE OF ERROR	**EXAMPLE**
OMISSION – one step of the tea-making sequence is missing	The step “add tea bag to mug” is missing
REPETITION – one step of the sequence is presented twice after some intermediate steps	The step “switch on the kettle” is presented twice, the first time after the step “add water to kettle” and the second time after the step “add sugar to mug”
VIOLATION – two steps of the sequence are presented in an illogical order	The step “add water to kettle” is presented after the step “switch on the kettle”

2.3 Procedure

2.3.1 *fMRI study*

The fMRI experiment was part of a larger project (Cogwatch FP7-ICT-2011-288912). Prior to completing the ASR task, participants completed a task which required them to produce a sequence of preparation of white tea with sugar by pressing a button box to put the steps in the correct order with the same pictures. The results of this study will be reported in a separate manuscript.

Before performing the ASR task in the scanner, all participants completed a training session. The session consisted of 8 randomized trials: 3 correct sequences, 4 incorrect sequences (two omissions, one repetition and one sequence error) and one scrambled sequence. Participants were asked to indicate if the presented sequence was correct or incorrect by pressing the 7 or 8 key respectively. No response was required to scramble sequences.

Four blocks including different sequences were presented during the fMRI session. Each block was composed by 18 trials (7 correct sequences, 9 incorrect sequences and 2 scrambled sequences) presented in random order. The sequences composing each block were selected so as to ensure the maximum equity between-blocks in the number of sequences depicting each tea-type and containing each error-type. Based on time availability with the use of the scanner, participants completed 2, 3 or 4 blocks of trials (two participants completed two blocks; 16 completed three blocks and one completed all four blocks). The order of the blocks presented was counterbalanced across participants. While they were in the scanner, participants were asked to mentally judge whether each tea sequence presented was correct or incorrect. An explicit manual response was not asked during the scanner session since we expected to find the activation of motor areas in relation to ADL sequence observation and the motor response of the participant could have implied a confounding activation. However, an explicit key-press response was asked at the end of 4 presented sequences in each block (at the end of 2 correct sequences and at the end of 2 incorrect sequences) in order to ensure that the participant was paying attention to the task.

The post-scan ASR task consisted of four experimental blocks (without the scrambled sequences) for a total of 64 trials. Participants made a correct or incorrect judgment by the end of each sequence by pressing the 7 or 8 key from the keyboard.

The online behavioural experiment was run using E-Prime 3.0 software. Participants were presented with the same sequences (*i.e.* 64 sequences) of the post-scan ASR task. In this case, instead of responding about the correctness of the whole sequence at the end of the trial, the participants were asked to respond about the correctness of each step. To do so, the participant had to respond after each step pressing the 7 key if the step was correct and the 8 key if the step was incorrect with respect to the task goal.

2.3.2 Scanning procedure

Participants underwent MRI scanning at the Birmingham University Imaging Centre (BUIC) on a 3 Tesla machine (Achieva, Philips). A sagittal T1-weighted sequence (175 slices, TE/TR=1/8.4s, voxel size 1×1×1mm) was used to acquire the anatomical scans. Whole-brain data were acquired using echoplanar imaging (EPI) sensitive to BOLD contrast (38 slices 2 mm thick with a 1 mm gap, tilted to align with the intracommisural plane, TE/TR/flip angle = 34.5ms/2.4s/80º, voxel size: 2.5x2.5x2 + 1 mm gap) with an EPI factor of 49. A field map was acquired using gradient echoes at 2.14 and 12.14 ms.

8.4. Plan Analysis

8.4.1 Analyses of behavioural data

Post-scan session behavioural data were analysed with repeated measure ANOVAs to compare accuracy and reaction times between the 4 different types of sequences (*i.e.* correct, omission, repetition and violation). Z-scores of RTs were calculated to account for intersubject variability.

Data derived from the online behavioural experiment were analysed in terms of step probability in ADL sequence knowledge. Based on normative data from 189 people performing the task of making tea, we previously calculated the probability of appearance of each step given the previous one (MDP probability). We calculated the percentage of times that each step was performed immediately following a specific step (or its likelihood of being performed as the first step). For example, we counted the percentage of times that the step "add water to kettle" was performed as the first step; the percentage of times that the step "switch on the kettle" was performed after the step "add water to kettle" and so on. This process led to the creation of 4 categories: 1) "High-probable" if the step's probability was >70%; 2) "Medium-probable" if the step's probability was ≤ 70% and ≥ 30%; 3) "Low-probable" if the step's probability was <30%; and 4) "Error" if it was the wrong step (see figure 8.1 for an example of correct steps with different probability levels). The average accuracy and z-score RTs for each step category were calculated and used as dependent variables in t-tests to compare High-probable to Low-probable and Error steps.

8.4.2. Analyses of the functional data set

The fMRI time series data were analysed with SPM12 software (http://www.fil.ion.ucl.ac.uk/spm/spm12.html) on a Matlab platform (Mathworks Inc.).

8.4.2.1. Preprocessing

EPIs were realigned and corrected for field distortion (Andersson et al., 2001), slice timing and head movement. AC-PC oriented (DARTEL imported) grey and white matter images were produced following the unified segmentation algorithm in the T1 images. DARTEL templates were created and each participant's EPI images were warped to the DARTEL template, then transformed to the MNI space and smoothed with an 8x8x8 full width at half maximum. The resulting EPI images were used as dependent variables in the following statistical analyses.

8.4.2.2. Statistical analyses

A mass-univariate voxel-based analysis was performed using a summary statistic with two levels: first and second. First-level analyses modelled the responses of each participant collapsing all the versions. In the first-level model covariates of no interest included: tea type, rare motor response events, the six movement parameters and harmonic capturing slow fluctuation in the signal (1/128 Hz). We used two different first-level models, each aimed at exploring different features of the design. The second-level analyses modelled participants as random effects and used a repeated measure design (including a regressor for each participant). A seed time course was obtained for the most significant cluster of interest by extracting the first eigenvariate.

8.4.2.2.1 Analysis 1: Correct and error type analysis – Mini-block-based

The first-level model included four separate regressors depicting the sequence correctness (*i.e.* correct, omission error, repetition error and violation error) and one for the scrambled sequences. Each regressor modelled the onset and duration of each trial (including all subtask steps). These onset regressors were convolved with the canonical haemodynamic response function. The resulting beta images corresponding to the types of errors and the correct trials were used as the dependent variable in the second-level analysis. Several t-test contrasts were performed to study cerebral activity related to sequence and sequence error processing. First, all types of sequences (*i.e.* correct and incorrect ones) were collapsed and compared to the scrambled sequence. Next, correct sequences were compared to incorrect ones (collapsing all types of errors). Finally, sequences containing different types of errors were compared to one another (*i.e.* Omission vs. Repetition vs. Violation).

8.4.2.2.2. Analysis 2: Step probability – Event-related design

The first-level analysis included five regressors modelling the onset of each event: high probability, medium probability, low probability, and surprise-error. These onset regressors were convolved with the canonical haemodynamic response function. The resulting beta images were used as dependent variables in the second-level analysis. A series of t-test contrasts was performed in which High-probable steps were compared to Low-probable and Error steps.

For all analyses, only significant clusters that survived Family-Wise Error (FWE) correction are reported ($p< 0.05$) with an uncorrected voxel threshold of $p < .0.001$.

8.5. Results

8.5.1 ADL sequence knowledge and error monitoring

8.5.1.1. Post-scan behavioural data

Accuracy and RT means and standard deviations of correct, omission, repetition and violation sequences are shown in Table 8.1. No significant differences were found for accuracy, F= 1.19, p= .327, η^2_p= .084. Significant RT differences were found between the four types of tea sequence trials, F= 5.66, p= .003, η^2_p= .303 (omission >* violation >* repetition = correct). The slowest responses were found for sequences with omission errors, followed by sequences with violation errors (t=1.48, p=.162, d'=.396), correct sequences (t=2.69, p=.019, d'=.719) and sequences with repetition errors (t=3.87, p=.002, d'=1.03). Responses to sequences with violation errors were significantly slower than responses to sequences with repetition errors (t=-2.89, p=.012, d'=-.775), and only marginally slower than responses to correct sequences (t=1.97, p=.071, d'=.526). No differences were found between correct sequences and sequences with repetition errors (t=.02, p=.985, d'=.005).

Table 8.2. Mean (standard deviation) of accuracy and reaction times in milliseconds in the post-scan ASR task

	Accuracy	RT
Correct	68.1% (33.4)	587.8 (336.7)
Omission	76.3% (19.8)	660.2 (281.7)
Repetition	85.2% (24.7)	546.2 (315.4)
Violation	80.8% (21.1)	555.6 (263.3)

8.5.1.2. fMRI data: Tea-making sequences monitoring

First, to replicate previous studies about ADL sequence monitoring, we contrasted tea-making sequences (collapsing correct and incorrect sequences) and the low-level control condition, that is, sequences with scrambled images. As expected, an increase in cerebral activation was observed for monitoring tea-making sequence trials in areas associated with the following: executive function and attention in the right inferior and superior frontal gyri; action and motor responses in the left precentral gyrus, posterior cingulate cortex, bilaterally in the medial superior frontal cortex, the supplementary motor area and posterior inferior parietal lobe; and high-level visual processes in the posterior middle temporo-occipital cortex and the insular cortex (see Table 8.3). The opposite contrast (*i.e.* Scrambled sequences > Tea-making trials) showed an increase in activation in bilateral medial occipital areas, the medial frontal area and left parietal cortex.

8.5.1.3. fMRI data: sequence error monitoring

No significant cluster activation was found in the Correct > Incorrect contrast. However, incorrect sequences, compared to correct ones, correlated with an increased BOLD response bilaterally in the ventral prefrontal cortex extending to the insula and in the posterior temporal lobe (see Table 8.4, grey shaded rows, and Figure 8.2).

When comparing the different error types, relative to omission errors, repetition and violation errors were associated with an increased response in the left prefrontal cortices, peaking in the superior frontal gyrus and extending to bilateral medial prefrontal structures, and in the bilateral inferior parietal cortex. Repetition errors compared to omission ones were also associated with responses of left subcortical regions including the basal ganglia and the hippocampus and extending to the insula and superior temporal cortices. Violation errors, compared to omission ones, were associated with an increased response in widespread bilateral frontal regions, from the superior frontal gyrus to the cingulate cortices (see Table 8.4 and Figure 8.2).

No above-threshold response was found in the Repetition > Violation, Violation > Repetition/Omission > Repetition/Violation contrasts.

Table 8.3. Regions of increased activation in Image > Scrambled sequences and Scrambled sequences > Image contrasts

Location	Coordinates	Peak z-value	Cluster size (#voxels)
Tea sequences > Scrambled sequences			
R IFG extending to R PreCG, MFG, SFG	42 9 30	4.96	311
L PreCG extending to L IFG, MFG	-39 0 33	5.07	553
R SMA extending to L SMA, SFG, right MedSFG	6 18 51	5.71	310
R ins. extending to R put., IOrbG	33 21 0	5.49	97
L ins. extending to L put., IFGtri	-30 21 6	4.64	77
L PCC extending to bilateral MCC and thalamus	-3 -30 24	4.97	143
R AG extending to R IPG, SPG, MOG, SOG, SprMG	36 -57 42	5.92	534
L IPG extending to L SPG, AG, PostCG	-30 -54 42	6.69	1152
R posterior MTG extending to R MOG, IOG, ITG	45 -72 0	5.67	212
L MOG extending to L IOG, MTG, ITG and FG	-45 -72 0	Inf.	570
Scrambled sequences > Tea sequences			
R IFG extending to R IOrbG, MFG	54 33 0	4.67	56
L MedSFG extending to L SFG, R MedFG, ACC	-9 66 18	6.46	1685
L PreCG extending to L PostCG, IPG	-39 -18 51	3.88	61
L AG extending to L MOG, MTG	-42 -69 30	5.87	231
L Rol. Op. extending to L STG, Heschl, MTG, MTP, STP, posterior OFC	-51 -6 9	5.72	1032
R calcarine extending to L calcarine, SOG, cuneus	6 -87 -3	Inf	6521

IFG = inferior frontal gyrus; PreCG = precentral gyrus; MFG = middle frontal gyrus; SFG = superior frontal gyrus; SMA = supplementary motor area; MedSFG = medial superior frontal gyrus; PCC = posterior cingulate cortex; MCC = middle cingulate cortex; ins. = insula; put. = putamen; IOrbG = inferior orbital gyrus; PostCG = postcentral gyrus; AG = angular gyrus; SprMG = supramarginal gyrus; IPG = inferior parietal gyrus; SPG = superior parietal gyrus; STG = superior temporal gyrus; MTG = middle temporal gyrus; ITG = inferior temporal gyrus; SOG = superior occipital gyrus; MOG = middle occipital gyrus; IOG = inferior occipital gyrus; FG = fusiform gyrus; Rol. Op. = rolandic operculum; OFC = orbitofrontal cortex

Table 8.4. Results based on trial correctness

Location	Contrast	Coordinates	Peak z-value	Cluster size (#voxels)
Frontal lobe				
R IFG extending to MFG, posterior OFC, ins.	Incorrect > Correct	45 36 -6	4.81	347
L IFG extending to lateral and posterior L OFC, STP, MTP, ins.	Incorrect > Correct	-39 30 -9	3.71	76
R anterior OFC extending to R MFG, SFG, MedSFG	Violation > Omission	27 45 -12	4.21	88
R SFG extending to R MFG, SMA, IFG, MCC	Violation > Omission	24 21 60	4.29	173
L MFG extending to L PreCG, SFG, IFG, bilateral MedSFG	Violation > Omission	-33 15 39	4.77	180
L SFG extending to L MFG, MedSFG, IFG, lateral OFC	Repetition > Omission	-15 45 36	4.30	66
	Violation > Omission	-24 54 9	4.16	124
L MCC extending to R MCC, L ACC, PCC	Violation > Omission	-3 -15 30	4.05	144
Temporal lobe				
R anterior MTG extending to L ITG, STG	Incorrect > Correct	63 -36 -3	4.48	167
L anterior MTG extending to L ITG, STG	Incorrect > Correct	-57 -36 -3	4.47	86
Parietal lobe				
R AG extending to R IPG, MOG, SprMG, STG, MTG, ITG, ins.	Repetition > Omission	51 -45 15	4.10	94
	Violation > Omission	48 -57 36	4.74	344
L IPG extending to L AG, SprMG, MOG	Repetition > Omission	-33 -45 27	4.83	75
	Violation > Omission	-45 -54 39	4.62	237
Subcortical				
L thal. extending to L GP, put., HC, Heschl, ins., STG	Repetition > Omission	-24 -21 0	4.12	63

SFG = superior frontal gyrus; MFG = middle frontal gyrus; IFG = inferior frontal gyrus; OFC = orbitofrontal cortex; SOrbG = superior orbital gyrus; PreCG = precentral gyrus; SMA = supplementary motor area; MedSFG = medial superior frontal gyrus; ACC = anterior cingulate cortex; MCC = middle cingulate cortex; PCC = posterior cingulate cortex; ins. = insula; STP = superior temporal pole; STG = superior temporal gyrus; MTP = middle temporal pole; MTG = middle temporal gyrus; ITG = inferior temporal gyrus; IPG = inferior parietal gyrus; AG = angular gyrus; SprMG = supramarginal gyrus; MOG = middle occipital gyrus; thal.: thalamus; GP = globus pallidus; put. = putamen; HC = hippocampus.

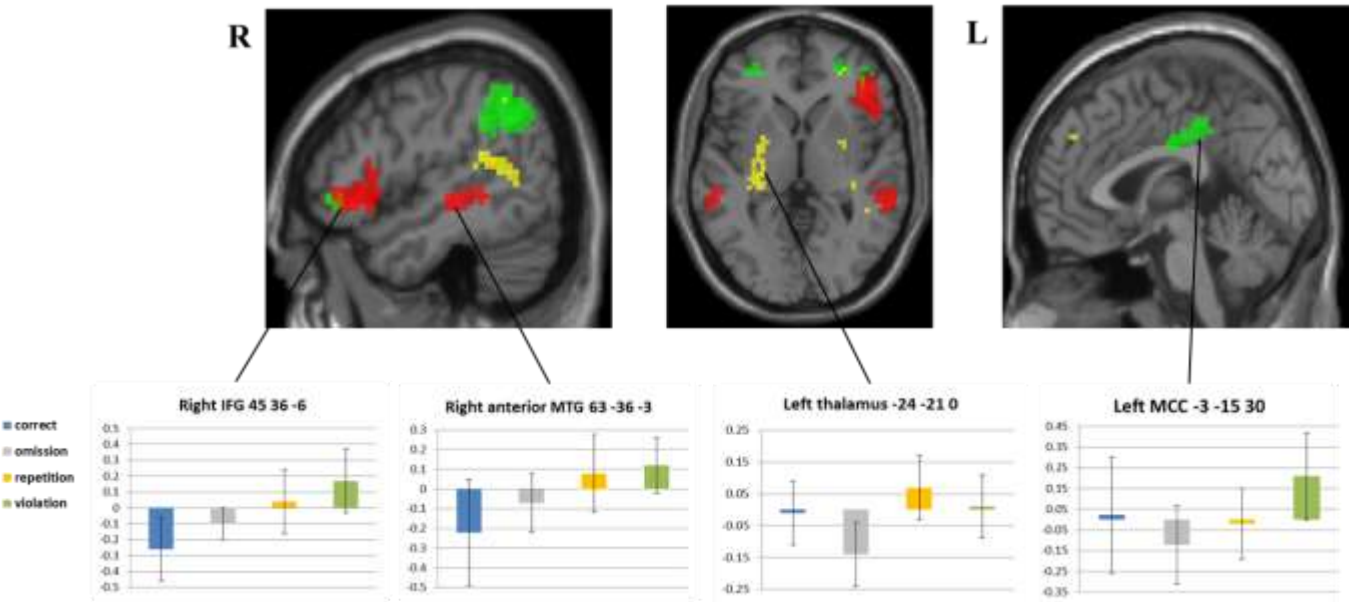


Figure 8.2. Increase in cerebral activation in the contrasts Incorrect > Correct (red blobs), Repetition > Omission (yellow blobs) and Violation > Omission (green blobs) and adjusted mean effect size of the four conditions (i.e. correct, omission, repetition and violation) in the right inferior frontal gyrus (IFG), right anterior middle temporal gyrus (MTG), left thalamus and left middle cingulate cortex (MCC). Error bars represent standard deviation of the mean.

8.5.2 Step predictability

8.5.2.1 Online behavioural study

Accuracy was significantly greater in high-predictable steps (94.3%) than in medium-predictable (80.1%), $t(1,25) = 6.14$; $p < .001$; $d' = 1.2$, low-predictable (71.5%), $t(1,25) = 7.8$; $p < .001$; $d' = 1.6$, and surprise-error steps (50%), $t(1,25) = 8.23$; $p < .001$; $d' = .25$. Accuracy in medium-predictable steps was significantly higher than in both low-predictable, $t(1,25) = 3.8$; $p < .001$, and surprise-error steps, $t(1,25) = 5$; $p < .001$. Accuracy in low-predictable steps was higher than in surprise-error steps, $t(1,25) = 3.5$; $p = .002$.

High-predictable (929.6 ms) and medium-predictable steps (938 ms) showed similar reaction times, $t(1,25) = -0.2$; $p = .846$, with both types of steps showing faster responses than low-predictable steps (1167.9 ms), $t(1,25) = -3.28$; $p < .001$; $d' = .35$ and $t(1,25) = -4.9$; $p < .001$, respectively, and surprise-error steps (1422.8), $t(1,23) = -6.62$; $p < .001$; $d' = .51$) and $t(1,25) = -7.9$; $p < .001$, respectively. Finally, responses to low-predictable steps were faster than responses to surprise-error ones, $t(1,25) = -5.1$; $p < .001$. In summary, as expected, predictability affected both accuracy and RTs; specifically, greater step predictability was associated with faster and more accurate responses.

8.5.2.2 fMRI data

High-predictable steps, compared to low-predictable and surprise-error ones, led to an increased response in the left precentral gyrus and bilaterally in the inferior parietal gyrus extending to the superior parietal gyrus, and posterior temporo-occipital cortex. This resembled part of the network previously found in responses to the tea-making sequence Image > Scrambled image processing contrast (see Table 8.5 and Figure 8.3). In the opposite contrasts (*i.e.* Low-predictable > High-predictable and surprise-Error > High-predictable), brain activation was observed in a different network, including medial frontal and occipital areas and the left superior frontal gyrus and the bilateral parieto-temporal junction and posterior parietal cortex (see Table 8.6 and Figure 8.3). Increased activation in the right prefrontal cortex including the superior, middle and inferior/orbital gyri was found in the Low-predictable > High-predictable contrast and activation in the left inferior frontal/orbital cortex only appeared in the surprise-Error > High-predictable contrast.

Table 8.5. Regions of increased activation in High-predictable >Low-predictable and High-predictable > surprise-Error contrasts

Location	Contrasts	Coordinates	Peak z-value	Cluster size (#voxels)
Left PreCG extending to MFG and SFG	High > Low	-27 -9 51	4.61	89
	High > Error	-39 -6 48	4.90	161
Right IPG extending to SPG, PostCG and AG	High > Low	30 -51 57	4.17	43
	High> Error	30 -48 54	5.24	151
Left IPG extending to PostCG, SPG and SprMG	High > Low	-30 -42 48	5.56	325
	High> Error	-30 -42 48	6.06	459
Right posterior MTG extending to R posterior ITG, IOG, SOG, MOG, cuneus	High > Low	48 -66 -3	6.77	752
	High> Error	48 -66 -3	Inf.	1116
Left posterior MTG extending to L posterior ITG, IOG, SOG and FG	High > Low	-45 -69 3	6.74	834
	High > Error	-45 -69 3	7.82	1124

SFG = superior frontal gyrus; MFG = middle frontal gyrus; PreCG = precentral gyrus; PostCG = postcentra gyrusl; SPG = superior parietal gyrus; IPG = inferior parietal gyrus; AG = angular gyrus; SprMG = supramarginal gyrus; MTG = middle temporal gyrus; ITG = inferior temporal gyrus; SOG = superior occipital gyrus; MOG = middle occipital gyrus; IOG = inferior occipital gyrus; FG = fusiform gyrus.

Table 8.6. Regions of increased activation in Low-predictable > High-predictable and surprise-Error > High-predictable contrasts

Location	Contrasts	Coordinates	Peak z-value	Cluster size (#voxels)
Left MedSFG extending to L SFG, MFG, R MedSFG	Low>High	-3 36 45	5.39	1618
+ extending to IFG, anterior and lateral OFC	Error>High	-6 39 39	5.54	557
Right MFG extending to right SFG, IFG, anterior and lateral OFC, SMedFG, ACC	Low>High	24 54 6	4.40	72
	Low>High	42 18 39	4.27	79
Left IFG extending to lateral OFC	Error>High	-51 21 3	4.20	131
Right anterior MTG extending to right STG and ITG	Low>High	60 -33 -6	4.88	165
	Error>High	60 -33 -6	4.97	219
Left anterior MTG extending to left STG and ITG	Low>High	-60 -33 -6	4.59	66
	Error>High	-60 -33 -6	4.36	111
Right AG extending to right SprMG and IPG	Low>High	45 -51 30	4.25	88
+ extending to STG	Error>High	60 -54 33	4.51	354
Left SprMG extending to L IPG, AG	Low>High	-57 -54 30	4.71	202
+ extending to MTG, STG	Error>High	-51 -54 30	4.74	216
Left LG extending to right LG and cuneus, bilateral calcarine and left cerebellum	Low > High	-9 -78 -3	4.69	1285
	Error > High	-9 -78 -3	6.57	2128

SFG = superior frontal gyrus; MFG = middle frontal gyrus; IFG = inferior frontal gyrus; ; OFC = orbitofrontal cortex; ACC = anterior cingulate cortex; IOper. = inferior operculum; MedSFG = medial superior frontal gyrus; STG = superior temporal gyrus; MTG = middle temporal gyrus; ITG = inferior temporal gyrus; AG = angular gyrus; SprMG = supramarginal gyrus; IPG = inferior parietal gyrus; LG = lingual gyrus.

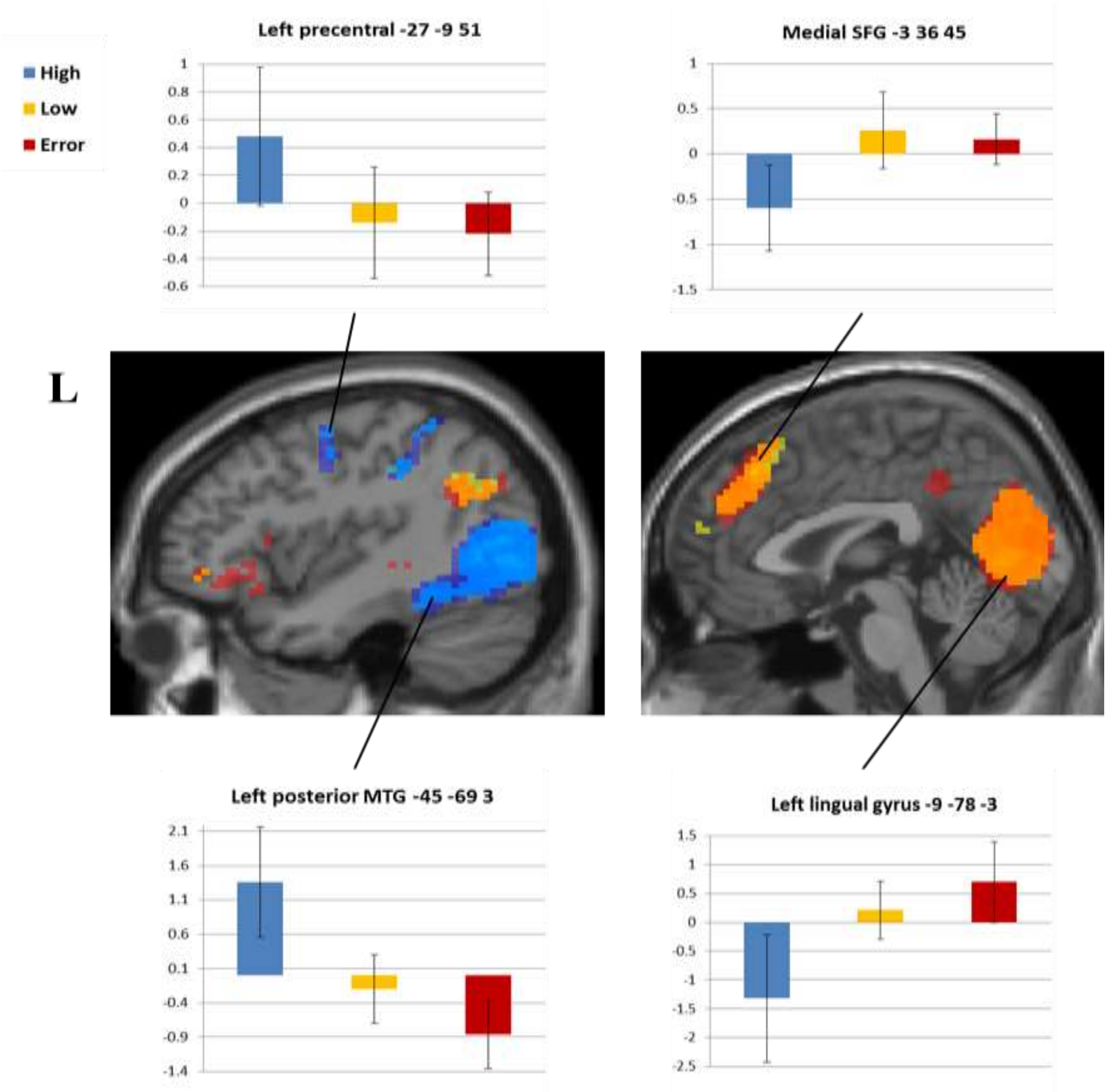


Figure 8.3. Increase in cerebral activation in the contrasts High > Low (light blue blobs), High > Error (dark blue blobs), Low > High (yellow blobs) and Error > High (red blobs) and adjusted mean effect size of the three conditions (High-predictable, Low-predictable and surprise-Error) in the left precentral gyrus, left posterior middle temporal gyrus (MTG), medial superior frontal gyrus (SFG) and left lingual gyrus. Error bars represent standard deviation of the mean.

8.6. Discussion

In the present study, we used functional neuroimage to identify brain networks supporting sequence knowledge and the monitoring of different types of steps and errors in familiar ADLs.

According to behavioural data, participants were faster at identifying correct sequences and repetition errors than incorrect sequences where the error was order violation or omission of steps. Regarding the steps themselves, responses to steps with higher predictability were faster and more accurate than those to steps with low predictability. Identifying surprise-error steps was most difficult for participants. Responses of the brain mirrored the dissociation observed in the behavioural results.

8.6.1 ADL sequence knowledge and error monitoring

As predicted and in line with previous studies (Crozier et al., 1999; Knutson et al., 2004; Krueger et al., 2007; Nemmi et al., 2013; Weiss et al., 2006), processing of tea-making sequences, compared to baseline non-action stimuli, was supported by a wide network bilaterally involving the middle and superior prefrontal, motor and supplementary motor areas, medial areas in the middle and posterior cingulate cortex, insular cortex, basal ganglia, superior and inferior parietal gyri and posterior tempo-occipital cortex. We refer to these areas as the "ADL network" (Cattaneo & Rizzolatti, 2015; Reynaud et al., 2019). These results confirm the involvement of both perceptual and motor processing and high-order functions in ADL monitoring. Therefore, as proposed by Hartmann et al. (2005), "It takes the whole brain to make a cup of [tea]".

Going beyond previous studies, we identified a specific network different from the ADL network involved in monitoring incorrect ADL sequences compared to correct ones. This ‘error ADL network’ included regions in the bilateral orbital and inferior prefrontal cortex, including the insula, and anterior temporal cortex. It is worth noting that, in contrast with the present study, previous studies have reported these areas in response to the observation of ADL sequences vs. baseline (Crozier et al., 1999; Krueger et al., 2007; Weiss et al., 2006). However, these studies did not directly compare incorrect and correct ADL sequences. Knutson et al. (2004) reported inferior prefrontal activation specifically in response to the sequential aspect of ADLs vs. category aspects (Knutson et al., 2004), suggesting that this area is relevant to validate the temporal order of ADL steps.

We did not observe any above-threshold response to correct vs. incorrect ADL sequences. This contrasts with Nemmi et al. (2013), who reported increased responses to correct trials in the right angular gyrus. In the current study, we recorded the involvement of the right angular gyrus in most analyses: in the processing of ADL sequences vs. scrambled sequences, in the processing of repetition and violation errors rather than correct sequences and during the processing of both high- and low-predictable steps when compared with one another. However, all these responses differed in the foci of activation, so the right angular gyrus could have multiple subdivisions with different functions (Seghier, 2013).

Violation and repetition errors (compared to omission errors) recruited the bilateral inferior parietal gyrus extending to the middle occipital gyrus and left superior and medial frontal areas. These results partially replicate previous literature according to which, compared to correct ADL sequences, incorrect ones are associated with an increased response primarily in high-order visual areas (*i.e.* middle occipital and fusiform gyri) (Nemmi et al., 2013). In contrast, we showed a much wider network response to incorrect sequences, including regions in the bilateral superior and inferior prefrontal, inferior parietal and anterior temporal gyri. This difference can be explained by considering differences in task difficulty. In the current study, we used variations of a single ADL (*i.e.* tea making) and embedded erroneous step in a sequence of 6-9 events (task accuracy was around 80%); while Nemmi et al. used a large variety of ADLs with fewer steps and where the errors were obvious.

The involvement of the extended network in sequence error recognition is in line with neuropsychological studies, in which patients with lesions in the prefrontal (Sirigu et al., 1995; Sirigu et al., 1996) temporal (Stephanie Cosentino et al., 2006; Emmanouel et al., 2016; Farag et al., 2010) and parietal cortex (Godbout et al., 2004) showed deficits in sequencing events and recognizing sequence error in ADL scripts.

An additional neural differentiation was found between the three types of errors. While repetition errors activated subcortical basal ganglia, violation errors activated the right superior prefrontal cortex and the middle cingulate cortex. These results partially replicate those of Weiss et al., (2006), who reported the same middle cingulate activation specifically in responses to sequence violation errors in ADLs rather than other error types (*i.e.* spatial errors). Surprisingly, we did not observe any areas specifically sensitive to omission errors. This is in contrast with previous neuropsychological studies (Bailey et al., 2013; Seidel et al., 2013) that reported the involvement of medial temporal areas and the hippocampus in omission errors. However, in those studies, actual performance, rather than the detection, of ADL errors were analysed. As in previous behavioural studies with neurological patients

(Giovannetti, Libon, & Hart, 2002; Morady & Humphreys, 2009) we found that, behaviourally, omission errors (with long reaction times and low accuracy) were the hardest to detect in terms of both accuracy and RT. It is unclear why such a condition that was so effective behaviourally had no reliable correlation with brain responses. In the current experiment, the ADL trials shared the main goal of making a cup of tea, with only the milk and sugar subgoals changing between trials. Hence, during the fMRI study, participants may have failed to detect an error when these subgoal steps were omitted. Another possible explanation is that, in a tea-making task, most steps can be performed at any point of the sequence (*e.g.* in tea with sugar, sugar can be added to the mug at any point of the sequence), thus failure to include a step can only be identified once the task is finished. It is a challenge in MRI to identify the time point of an absent event.

This error type analysis confirmed the existence of qualitative differences in the processing of different types of sequence errors in naturalistic tasks. This differentiation partially supports the commission (including violation, repetition and object substitution) vs. omission categorization proposed by Giovannetti et al., (2008), with the bilateral superior frontal and inferior parietal gyri showing sensitivity to any commission error as opposed to an omission error. However, dissociations within commission errors were also observed behaviourally and neuronally, suggesting that subdivisions should be made within the commission category.

In summary, we showed that a specific ‘error network’ including the bilateral orbital and inferior frontal cortex, the insula and anterior temporal lobe was sensitive to incorrect ADL sequences. Among incorrect sequences, the bilateral inferior parietal and superior frontal gyri extending to the middle frontal gyrus were mostly sensitive to repetition and violation errors relative to omission ones. Finally, the cingulate cortex and right superior lateral frontal gyrus responded specifically to violation errors and the basal ganglia and hippocampus responded to repetition errors.

8.6.2 Step predictability

High-predictable (relative to low-predictable and surprise-error) steps activated the bilateral posterior middle temporal extending to the occipital cortices, the inferior parietal gyrus extending to superior parietal cortex and the left precentral gyrus, overlapping with part of the ADL network reported above (Reynaud et al., 2019).

Again, a different network supported low-predictable and surprise-error events. Compared to high-predictable events, low-predictable and surprise-error events were associated with increased activation in the bilateral anterior temporal, superior and medial prefrontal cortices and inferior parietal, lingual and right inferior frontal gyri (Table 8.5). The involvement of the medial frontal-occipital network in response to low-predictable and surprise-error steps is congruent with previous studies that have reported the activation of these areas in response to unexpected events (Schiffer et al., 2014; Schiffer & Schubotz, 2011) and incorrect sequences (independently of the type of stimuli, Nemmi et al. 2013). The anterior temporal and right orbital cortices observed in the low-predictable events overlapped with the observed foci responding to incorrect (vs. correct) trials (Table 8.3). This suggests that these areas did not encode errors per se but were involved in processing events with low predictability. Similarly, the areas in the bilateral superior and middle and medial prefrontal cortices and the bilateral inferior parietal gyrus (including the right angular gyrus) which showed sensitivity to violation and repetition errors were also likely to be involved in processing unexpected actions. The involvement of early visual regions including the lingual gyrus and calcarine was observed only when we modelled the data as events. This suggests that there may be temporary recruitment of early visual processing when an unexpected event occurs. The extra sensory processing is potentially used to validate the unexpected percept. Finally, the only area that was sensitive only to the surprise-error event was the left inferior frontal gyrus extending ventrally to the orbital cortex (also found in the incorrect vs. correct sequences analysis). This suggests that this area may be directly involved in error detection, irrespective of event predictability.

8.6.3 Limitation and methodological considerations

Some limitations must be acknowledged. Sample size was relatively small (N=19), especially for fMRI studies. This means that only large effect sizes could be reliably detected. In addition, the sample was mainly composed by young, right-handed female students, which can affect the generalizability of the results.

The current experiment used a single ADL: making tea. Using variations on a single ADL meant that this put an extra demand on working memory, task switch and executive function. Further studies should extend the results of the present study and explore their generalizability to other familiar ADLs.

In the fMRI experiment, participants did not give an explicit response to sequence correctness. As we expected motor and premotor area activation in response to our task, requesting a response for each trial could have been a confounding source for such activation. Hence, we do not have an indication of participants' perception during the scanning. However, the accuracy observed in the post-scan session indicates that participants had high rates of sequence error recognition during the task.

Apart from these limitations, we consider that several strengths in the present study enhance its ecological value. First, the use of pictures with a first-person perspective is more ecologically valid. It also mimics the participant's perspective while executing the task and hence is more tightly linked to ADL processes and their embodied nature (Ivanova et al., 2021). This enables the recruitment of the action observation network (Kockler et al., 2010). Second, we used sequences composed of 6-9 images, depicting all the steps necessary at the same hierarchical level to achieve the task goal. Previous studies used steps representing high level goals that are ADLs per se (*e.g.* getting dressed) (Crozier et al., 1999; Krueger et al., 2007) or pertaining to the very low level of hierarchy (*e.g.* fold a napkin) (Manthey et al., 2003; Weiss et al., 2006). We used all the steps pertaining to the same intermediate level of subgoal, which is the level where most sequence errors occur and where step monitoring highly depends on executive functions. Similarly, the sequential presentation of the images increases the relevance of the steps' temporal order and the requirement of working memory in step monitoring. All these aspects are more ecologically valid and realistic.

8.6.4 The bigger picture

The results of the present study represent a step forward in the understanding of the neurocognitive mechanisms underlying sequence knowledge and ADL sequence monitoring. We identified different networks, each with a unique role in ADL processing (see Figure 8.4).

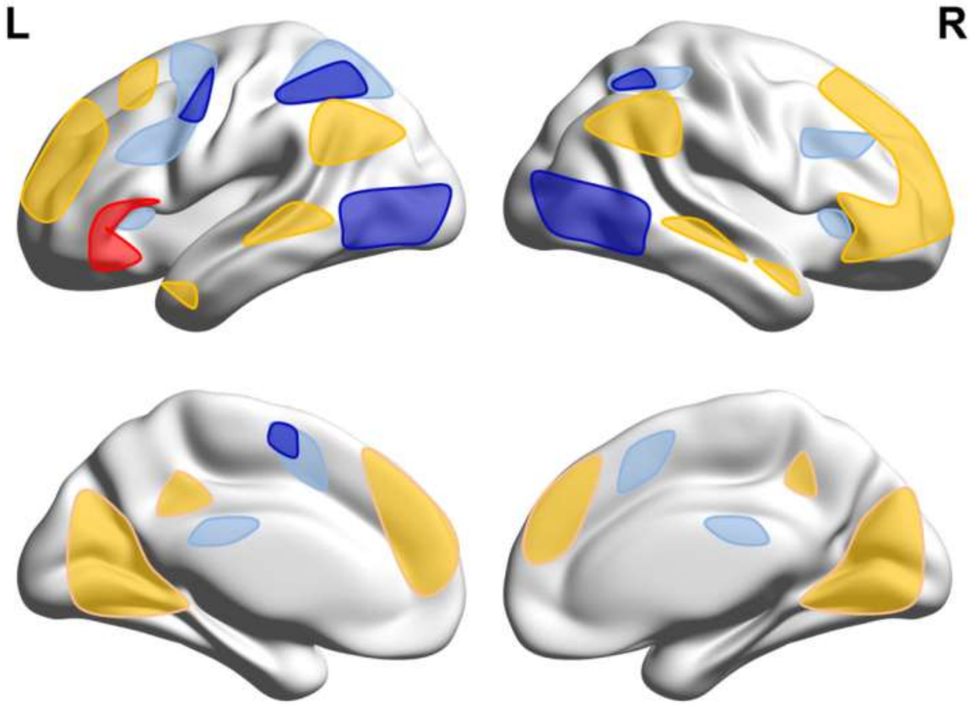


Figure 8.4. Brain model illustrating the action observation network (light blue), the overlapping high-predictable step network (dark blue), the low-predictable step network (yellow) and the area responding to errors (red).

First, a posterior dorsal network including bilateral posterior temporal areas and the middle occipital, left fusiform, bilateral inferior parietal and left precentral gyri was involved in processing highly expected action steps (dark blue areas in Figure 8.4). Not surprisingly, this network overlapped with the action observation network (light blue areas in Figure 8.4). The right orbitofrontal, bilateral superior and medial frontal, anterior temporal and inferior parietal cortices and medial occipital areas showed sensitivity to erroneous sequences and unexpected actions (yellow areas in Figure 8.4). Thus, we suggest that this network processes unpredictable events such as errors. Finally, areas in the ventral part of the left prefrontal cortex appear to be specifically sensitive to erroneous actions that hamper the success of the ADL task (red area in Figure 8.4).

Our data showed that it is important to consider event predictability when exploring the neural correlates of ADL sequences. This is because low-predictable events elicited similar responses to those of erroneous events. Furthermore, event predictability as defined by the MDP was highly informative for understanding behaviour and brain response. The different cognitive mechanisms underlying the execution and monitoring of high- and low-predictable steps can provide support to the contention scheduling model (Norman and Shallice, 1986). This model proposes that two different mechanisms underlie action selection in routinized and non-routinized tasks. While routinized tasks are automatically executed without the need to recruit frontal functions, non-routinized tasks require additional monitoring and attentional control processes typically hosted in the prefrontal cortices. In line with this, our results suggest that it is not just task familiarity that affects the monitoring (and potentially the execution) of ADL sequences but also the presence of expected vs. unexpected events (such as unpredictable steps and errors) occurring during these familiar situations (Norman and Shallice, 1986). Congruent with this idea, the network that monitors unexpected events (unpredictable and error steps) in the present studies comprehend areas of the monitoring system network previously found in response to errors (Agam et al., 2011;

Hester et al., 2005; Klein et al., 2007), conflicts (Cohen, 2014; Li et al., 2017) and uncertainty or low confidence judgment (Boldt & Yeung, 2015; Holroyd & Yeung, 2012a; Yeung & Summerfield, 2012) all situation in which the routine action is compromised.

The ability to detect omission, repetition and violation errors showed different behavioral and neural responses, pointing out the need to be studied separately, since different cognitive mechanisms may underlie their execution and detection. No areas showed sensitivity to detect omission errors, which were the most difficult to detect. The detection of violation errors were specifically associated with responses in the right superior frontal and middle cingulate cortices. Finally, repetition errors, which were rapidly and easily detected, were associated with response in left subcortical areas, including the basal ganglia and hippocampus.

We propose that qualitative differentiations based on sequence error types and step predictability can enhance the understanding of the error pattern of patients with neurological alterations. On the one hand, it is important to evaluate the types of errors that the patient performs and which types of errors the patient has more problems to detect. This information might help to better comprehend the cognitive processes that might be affected in a given ABI patient and guide the selection of appropriate intervention strategies. On the other hand, another aspect that should be taken into account when evaluating patients' performance is steps predictability which might be an important index of patients' cognitive deficits. This has important clinical implications and can further highlight potential avenues for rehabilitation, for example by creating ADL routines that maximize the number of highly predictable steps, for patients who make many sequence errors.

8.7. Conclusions

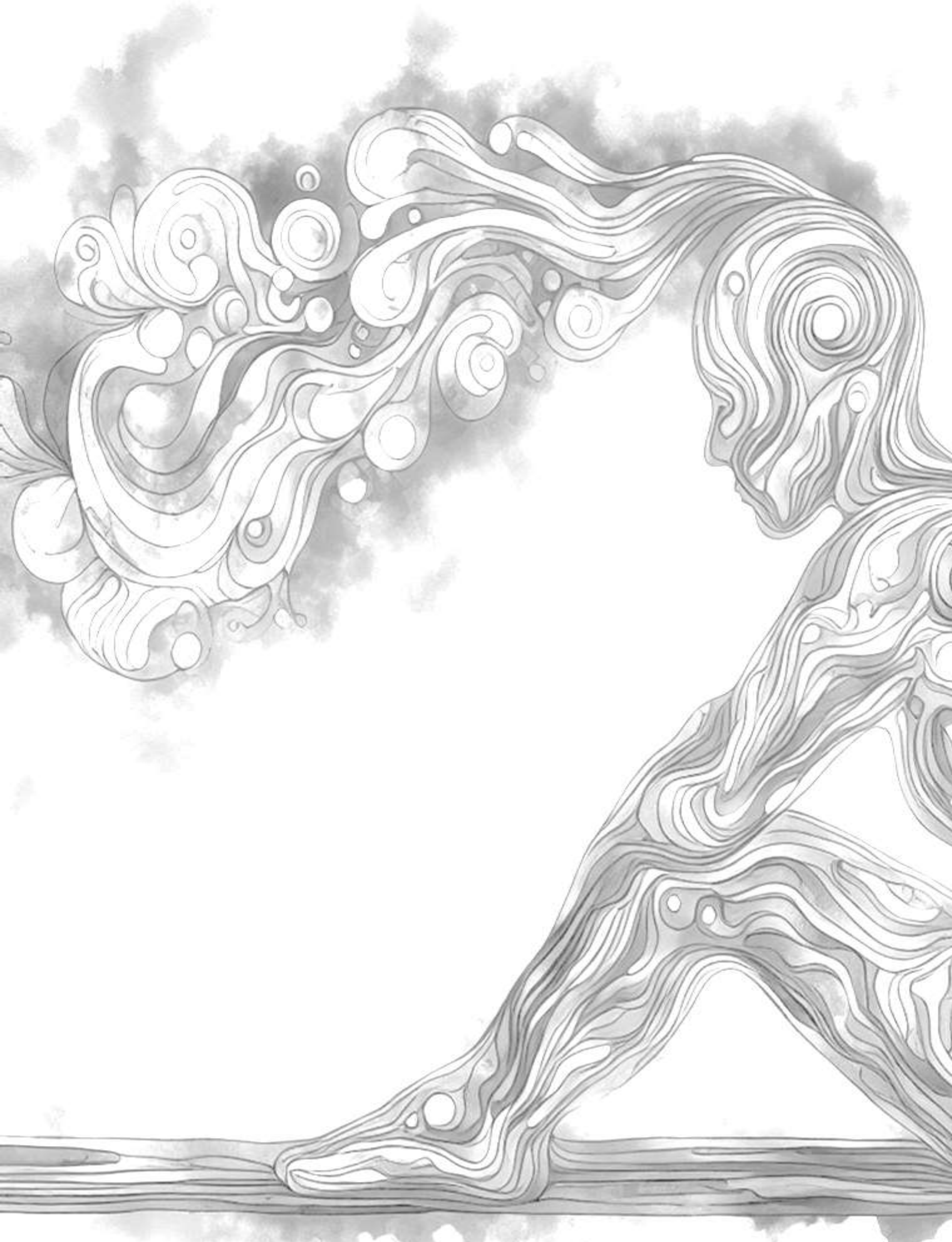
The present study shows that different networks in the brain are involved in monitoring different events during ADL sequence processing. Within the wide network that responds to ADL sequence, perceptual and motor areas process actions that are highly predictable. In contrast, the processing of unexpected events relies on a network including high functions and attentional areas in the bilateral anterior temporal, inferior parietal and superior frontal cortex and medial prefrontal and occipital regions. Finally, the left ventral frontal cortex specifically detect erroneous actions that might affect task goal achievement. Different network are involved in detecting different types of errors, with neural responses being more sensitive to commission errors (the execution of an erroneous action) than omission errors, supporting the commission-omission errors model. Extending this model, within the commission errors different areas process violation (right superior and ACC) and repetition errors (left subcortical areas), suggesting that their detection relies on different neural and cognitive mechanisms.

8.8. Aknowledgments

The present study was supported by the European Commission under grant FP7-ICT-2011-288912 (CogWatch) and BBSRC BB/R003971/1 to AW. GR was supported by the Spanish Ministry of Science, Innovation and Universities within the FPU program (FPU17/02536).

PART IV

DISCUSSION AND CONCLUSIONS



CHAPTER 9

GENERAL DISCUSSION

9.1. Summary of findings

The general aim of this dissertation was to provide new data to better understand SA and its alterations after ABI, and the nature of its components in the context of ADL. Different aspects of SA and of its relation with ADL have been addressed in the three studies. In general our results suggest that, not only it is possible to study specific components of SA in the context of ADL, but that it is also necessary, since ADL tasks confer to the study of SA an unique and significant perspective that cannot be grasped with other kind of tasks.

In **Study 1 (Chapter III)**, we based on the need of improving the *assessment of online components of SA* in the context of familiar, well-known ADL. We provide preliminary evidence of the validity of an ADL-based assessment protocol (previously published in Merchán-Baeza et al., 2020) to assess the online components of SA in patients with ABI. The findings of this study reveal that, through the observation of patients' performance in an instrumental (i.e. prepare a breakfast) and a basic (*i.e.* getting dressed) ADL, it is possible to specifically evaluate several online SA components at a time within the same individuals. As hypothesized, the online SA measures of emergent awareness and self-evaluation correlated with traditional measures of online SA in both tasks. Moreover, the results of this study also suggest that the present protocol seems a valuable tool to investigate unsolved questions about SA highlighted by recent reviews in the field (Sansonetti et al., 2022; Toglia & Goverover, 2022), such as the dynamic interaction among the online components of SA and the offline metacognitive component or the effect that cognition and task's complexity have on online SA. In fact, the findings of significant correlations between the emergent and anticipatory awareness indexes derived from the BT and measures of offline SA, are fully congruent with the DCMA (Toglia & Goverover, 2022; Toglia & Kirk, 2000). In addition, the different pattern of results found between the BT and the DT suggests, in accordance with previous research, that online SA varies depending on the task that is being taken into consideration. Based on our findings online SA seems to be more impaired in the context of more difficult tasks after an ABI. In addition, online SA impairments in easier tasks might be more influenced by general cognitive deficits. **Study 1** also has a direct implication for clinical practice, since it might offer a valid and easy-to-use index of online SA based on the coding of behavior restricted towards a given number of evoked situations to deal with distractors and conflicts present in each ADL task.

In **Study 2 (Chapter IV)** we analyzed in more detail the cognitive processes that underlie online and offline SA. More specifically, the aim of this study was to investigate whether *conflict monitoring* is one on the EF components that is mostly related to *emergent and offline SA*, given the apparent link identified between these components in previous theoretical models (Nick Yeung et al., 2004). However this link has been rarely studied in empirical research directly in the context of anosognosia. To study this relationship, a group of ABI patients with Severe-ISA, patients with No/Low-ISA and HC performed an experimental interference-based task that allowed simultaneously measuring three types of conflicts (*i.e.* the presence of distractors, Stroop and Simon conflicts). The results indicated that, in this task, Severe-ISA patients presented a significant conflict monitoring/resolution impairment compared to patients with No/Low-ISA and HC. In addition, we found that the ability of monitoring and solve some types of conflicts (*i.e.* the presence of distractors and the Simon conflict) significantly correlated and predicted offline and online emergent SA in ADL contexts.

Study 3 (Chapter V) zooms in on the neural mechanisms that underlie emergent awareness, the monitoring of ADL sequence and the recognition of different types of sequence errors. In this study participants observed different tea-making sequences that could be either correct or contain a sequence error (*i.e.* omission, repetition or violation) and had to judge their correctness. The results showed that different brain areas monitor for different types of error when observing ADL sequence. While no specific areas responded to omission errors, the bilateral superior frontal and inferior parietal gyri were sensitive to commission errors of repetition and violation. Additionally, specific responses to repetition errors were found in subcortical basal ganglia and hippocampus, while the cingulate cortex and the right superior frontal gyrus responded specifically to violation errors. In this study we also explored whether steps predictability affects sequence monitoring. Behaviorally, we found that the monitoring of highly predictable steps is easier than the monitoring of low predictable or erroneous steps. Similarly neural activity showed that the monitoring of highly predictable steps is supported mainly by perceptual and motor areas related to action observation. In contrast, the processing of low predictable and erroneous steps depends on a different network including areas in the right orbitofrontal, bilateral superior frontal, anterior temporal and inferior parietal cortices and in the medial frontal and occipital areas usually associated with processes of monitoring and attentional control.

The findings presented in this dissertation constitute valuable pieces of information that enhance our understanding of ISA, especially in the context of ADL. This information has relevant theoretical so as practical implications that are going to be discussed in the next sections.

9.2. Improving the assessment of self-awareness in patients with acquired brain injury

9.2.1. Toward an ecological evaluation of self-awareness

The present dissertation addresses the need of developing more ecologic evaluation tools for the study of SA. The use of Neuropsychological tests is highly valuable, since they permit to isolate and selectively evaluate in a very specific manner, the cognitive process we want to focus on during the evaluation. In addition, this type of assessment tools, throughout the creation of abstract stimuli and content, attempt to create the ideal condition to evaluate each cognitive domain eliminating the effect of extraneous variables (Harvey, 2012). Nevertheless, the same aspects that can be considered advantages in one respect can be considered as disadvantages when looking from a different perspective (Burgess et al., 2006). In fact, the performance in these types of tasks may not fully reflect the possible cognitive alterations as observed in daily life that affect patient's functionality (Burgess et al., 2006; Chan et al., 2008; Shallice & Burgess, 1991). The fact that the neuropsychological tests eliminate all the characteristics typical of naturalistic environment entails that the patient cannot rely on previous learning and real-world knowledge to face the task. This may lead to the overestimation of patients' cognitive deficits (Robertson & Schmitter-Edgecombe, 2017; Romero-Ayuso et al., 2019). In contrast ADL-based tasks, since they actually recreate in the laboratory similar situations that the patient has to face in the real world, may allow for the evaluation of the real impact that cognitive impairments have in patients functionality and daily living (Brunswik, 1955; Pinto et al., 2023; Spooner & Pachana, 2006).

Therefore, studies as the ones presented in this dissertation are highly valuable since might provide support to the potential validity of ADL-based task to study specific cognitive processes, such as online SA, within a similar naturalistic context that patients have to face in their real life. Nevertheless, the present dissertation also supports the idea that the combination of different methodologies in the investigation of cognition may help to address the drawbacks inherent of each technique. In fact the combination of methods that permit to isolate and measure in a fine grained basis a specific cognitive mechanism of interest and to relate it with more ecological measures may lead to a richer understanding of SA. In fact the use of more ecological measures may help to understand how the specific cognitive components assessed with experimental tasks or neuropsychological tests affect daily activities and functionality. In turn, the results of experimental tasks and neuropsychological tests may help to understand the cognitive mechanisms that underlie specific behaviors observed in the performance of daily activities (Culbreth et al., 2020; De Luca et al., 2018; Overmeyer et al., 2021).

9.2.2. Evaluation of self-awareness components

The importance to evaluate the online components of SA has been highlighted in the introductory chapter (Chapter 3). Given the fact that SA might depend on separate processes (*e.g.* emergent awareness, self-evaluation and updating) it is necessary to understand which specific deficit is actually most responsible of anosognosia in a given patient. The protocol presented in **Study 1** is an ADL-based assessment tool that was designed to provide a measure of all potential processes that might produce anosognosia, within the context of familiar and significant ADL tasks. Therefore, it has the potential to become an useful measure to validly assess online components of SA for both clinical and research purposes.

The protocol presents several advantages for the assessment of online SA compared to prior proposals. Firstly, the inclusion of an IADL and BADL allowed assessing online SA in the context of two tasks with different levels of complexity. This is an added value to the evaluation tool, since, as previously stated, SA could depend on the characteristic and complexity of the task (Fleming & Strong, 1999; Prigatano et al., 1986; Toglia & Goverover, 2022; Toglia & Kirk, 2000). As far as we know, it is the first time that a structured online SA evaluation protocol includes a BADL. We believe that the inclusion of a BADL in the evaluation protocol is particularly relevant, as it allows the assessment of online SA even in more severe patients who may have limitations in performing instrumental activities.

At the same time, the introduction of distractors and conflicting situations in both tasks, might have helped to increase the monitoring demands of the task, and to enable the evaluation of high cognitive processes, such as online SA, even in a simple basic task such as getting dressed. The presence of distractors and conflicting situations, because of increasing the monitoring demands it might also allow the use of this protocol even with participants that show mild decline or those that because of having so much practice performing these tasks they would produce very few or no errors in these kind of ADL if distractors and conflicting situations were absent. Indeed, how can we assess error detection and correction if the patient does not commit any errors? That was the problem found in several previous studies, where it was reported that it was not possible to assess online awareness for some participants due to a lack of mistakes during task performance (Schmitter-Edgcombe et al. 2021). However, The *Breakfast and Dressing Conflict Task* presented here seem not to have this problem, given the observation of high variability in the rate of overt errors even in healthy participants. This finding strongly suggests that this tool might be useful to identify subtle online SA problems even in healthy population, detecting mild cognitive impairments and decline. Previous studies, investigating the effect that the age-related cognitive decline have on ADL performance usually found that older participants, compared to young participants, showed performance impairments within the context of ADL tasks only when analyzing subtle behaviours, such as “microerrors”, efficiency scores, etc. (Giovannetti et al., 2019; Rycroft et al., 2018; Schmitter-Edgecombe et al., 2021; Seligman et al., 2014), while no differences were found when analyzing overt errors’ rates.

These aging findings contrast with preliminary results found in a recent aging study run in our laboratory with the *Breakfast and Dressing Conflict Task* comparing the performance of a group of young and old neurologically intact adults. According to this, we found differences among young and old participants not only in subtle microerrors but also in overt ones. Even further, we found that *Conflict-monitoring-index* significantly differed between groups in the *Dressing task* and significantly correlated with performance in EF tests in both tasks (Navarro-Egido et al., *in preparation*).

Taking together, we can conclude so far that the *Breakfast and Dressing Conflict Task* makes a good balance between the advantages of presenting two ADL tasks that are highly familiar and therefore applicable to most ABI patients but at the same time allowing to measure high level processes such as online SA.

Finally, the presence of distracting/conflicting situations led to limited and predictable types of potential errors to be coded and specific corrective actions. The observation of online SA restricted to these *evoked* situations of potential error (instead of measuring all potential *spontaneous* instances of them) may help to simplify the coding requirements, with potentially relevant advantages for future clinical practice. This is an important issue, since assessment tests based on ADL, even if they provides very rich and ecologically valid information about patients cognitive deficits, are not typically included in the clinical practice, because of being highly demanding in terms of coding and interpretation (Giovannetti et al., 2019).

Unfortunately, the updating measure included in our protocol through the requirement to assess the performance 30 minutes later after finishing each ADL task to assess mnemonic influences on SA, did not work properly, as it showed little variance in both tasks. This pattern may be due to an empirical issue rather than to the lack of validity of the strategy used to measure this component (*i.e.* the difference between the immediate and delayed self-evaluation of the performance). On the one side, as suggested in the discussion of Study 1, it is possible that the time span between the immediate and the delayed self-evaluation was not enough to detect the decay of the information about the performance in ABI patients (Ansell & Bucks, 2006; Stewart et al., 2010). Another possibility for the lack of variability might be the characteristic of our sample of ABI patients. In this sample, ISA could be primarily caused by emergent awareness deficits present in most patients, while very few patients actually exhibited updating problems. This problem may be enhanced by the fact that this index was only available for few patients (15 patients in the BT and 13 patients in the DT) and the probability of this subsample to be composed by a considerable number of patients with updating deficits was low. Therefore, future studies should test the validity of this updating measure with a larger sample and/or in other neurological pathologies, where ISA may be most closely associated to updating problems (*e.g.* Alzheimer's disease). Finally, the type of self-evaluation tool used (*i.e*. Likert-scale) could have influenced this finding. In fact, some patients, when asked for the delayed self-evaluation, correctly repeated the number said in the immediate self-evaluation (*e.g.* 2 = I could do it, but I made some mistakes). However, when asked for *which errors* they made, they could not recollect them. So we suggest that a qualitative, apart from a quantitative, assessment may be more sensitive to detect updating problems due to memory deficits. Given the importance of the updating component for SA and its implication in some forms of anosognosia such as the "petrified self" condition, it is important to further investigate this component and outline a more feasible updating measure.

By including a valid evaluation of the updating component the *Breakfast and Dressing Conflict Task* may be used in clinical practice to identify different profiles of anosognosia, discriminating whether the patient's ISA is caused by online emergent awareness impairments or by the failure in updating the metacognitive self-knowledge. As we will see below, this information is essential for designing appropriate rehabilitation strategies, which need to be tailored differently when addressing these two distinct profiles of anosognosia.

The present dissertation apart from offering preliminary validity data of an ADL-based protocol to assess online SA, responding to the issues observed in previous assessment tools and with potential benefits for clinical practice, open up new avenues of research of SA in the context of ADL that are going to be next discussed.

9.2.3. Qualitative assessment of emergent awareness

The identification in **Study III** of different cerebral network in response to the detection of different types of sequence errors suggests that different cognitive mechanisms underlying the error detection depending on errors characteristics. This finding highlights the need to incorporate a comprehensive qualitative evaluation of emergent awareness, as different brain lesions may lead to difficulties to identify different types of ADL sequence errors.
Omission errors are among the most difficult errors to be detected (also confirmed by the behavioral data of Study 3 and by previous behavioral ADL studies (Giovannetti, Libon, & Hart, 2002; Norman, 1981). The difficulty to detect omissions may reside in the fact that in this type of errors, due to the lack of the activation of the needed action, the mismatch (or conflict) between the intended and the actual action is not generated (Giovannetti, Libon, & Hart, 2002; Goldberg & Barr, 1990; Norman, 1981). Since this conflict detection mechanism may subserve error detection, its absence leads to a more difficult detection of the error. This lack of conflict may be reflected in the brain by the absence of a specific neural response to this type of error. In contrast, this mismatch detection may be reflected by the specific neural activation found in response to commission errors (*i.e.* repetition and violation vs. omissions), which may facilitate the detection of these types of errors.

In addition, within the category of commission errors, qualitative differences were found between repetition and sequence violation errors. On the one hand, the detection of repetition errors might involve short-memory and working memory processes; as suggested by the activation of the basal ganglia and hippocampus (Frank et al., 2001). In fact, this type of error might be detected when, based on the short-term history of sequence events, the person observes a step that has been already performed. On the other side violation errors elicited specific activation in the cingulate cortex and the right superior frontal gyrus, areas usually associated with conflict monitoring and resolution. Therefore, this type of sequence error might be detected based specifically on the recognition of a mismatch between the wrong sequence of steps observed and the correct sequence stored in semantic memory.

We are aware that all these hypotheses are based on inverse inference, that is, the assumption that a specific cognitive process is acting based on the neural activation, and should be taken with caution (Henson, 2005; Poldrack, 2006). Further research is needed in order to confirm the specific cognitive processes that underlie the detection of each type of sequence error.

The finding of different neural responses to different sequence errors add evidence to previous neuroimaging studies that also observed specific areas in response to non-sequence error. For example, the detection of visuospatial errors seems to be supported by a network including the right posterior and inferior parietal cortex, the middle temporal gyrus, the ventrolateral premotor cortex and the thalamus (Manthey et al., 2003; van Elk, 2014; Weiss et al., 2006) while the detection of sequence errors elicited specific activation in the middle frontal gyrus (Manthey et al., 2003). These previous studies, together with the Study 3 presented in this dissertation, show that evaluating error detection in the context of ADL is a promising approach. In fact, when studied in the context of experimental tasks that usually involve a unique cognitive domain and a unique type of error, error detection has been typically associated with the activity of the ACC and parietal and insular cortex (Agam et al., 2011; Fiehler et al., 2004; Hester et al., 2005; T. A. Klein et al., 2013; Van Veen & Carter, 2006). However, based on the study of error detection within ADL-based tasks it is feasible to suggest that, depending on the features characterizing each error, additional specific neural networks and mechanisms may be involved in error detection.

It is worth noting that while neuroimaging studies using experimental tasks have investigated the detection of errors made by the participants themselves (Agam et al., 2011; Fiehler et al., 2004; Hester et al., 2005; T. A. Klein et al., 2013; Van Veen & Carter, 2006), neuroimaging studies using ADL-based tasks focus on the detection of observed errors but not committed errors (Manthey et al., 2003; Nemmi et al., 2013; Weiss et al., 2006). Previous research suggest that self-perception and other-perception of action is supported by both shared and different neural systems (Decety & Sommerville, 2003; Jeannerod, 2003; Kockler et al., 2010; Ramnani & Miall, 2004). In line with this, it has been observed that some patients with anosognosia may be able to recognize a problem in another person, even if they are not aware of the same difficulty when they are involved themselves (Bertrand et al., 2016). This might be one of the reasons why intervention strategies based video feedback, where the patient watches in third-person perspective videorecordings of their own performance, is one of the most effective rehabilitation strategies used to address ISA (Engel et al., 2019; Fotopoulou et al., 2009; Schmidt et al., 2013; Villalobos, Bilbao, et al., 2020). Therefore, the finding that distinct cerebral areas are associated with the identification of different error types revealed in studies where participants observe errors made by others, remains valuable. In fact, based on the patient's lesion pattern, it might be possible to predict the effectiveness of a video feedback-based intervention or determine whether considering an alternative strategy would be more appropriate. Nevertheless, future studies should investigate whether areas similar to those identified in Study 3 (and previous ADL-based neuroimaging studies) are also engaged in detecting the same types of errors when they are committed by the participants.

Overall, the qualitative neural differentiation in error detection based on error types is congruent with the notion that distinct patterns of behaviors and errors are linked to diverse cognitive impairments and neural alterations (Bailey et al., 2013; Giovannetti et al., 2006; Niki et al., 2019; Seidel et al., 2013; Wulff et al., 2015, 2016). Nevertheless, this finding also opens new avenues for research. Prior studies have primarily focused on exploring the association between error patterns and cognitive deficits or cerebral lesions. However, future studies should investigate whether different brain lesions and cognitive impairments are also linked to the inability to recognize specific types of errors. If such associations are identified, evaluating which types of errors the patient cannot detect could serve as an index to better comprehend the patient's cognitive deficits and ISA profile and how these impairments influence the patient's daily activities.

Nevertheless, we acknowledge that studying the cognitive and neural correlates of the detection of different types of errors during ADL performance may entail several challenges. An important consideration is that error detection analysis typically relies on verbalization and/or behaviors that indicates that the patient has detected the error, leaving uncertainty about their true awareness level (Bettcher et al., 2008) and whether some instances of detections occurred but they are unnoticed because patient don't produce any of these overt behaviors. One solution to this problem that would allow to obtain more direct measures of error detections may come from neurophysiological and neuroimaging measures (*e.g.*, EEG, skin conductance, pupilometry, fMRI, etc.) that can assist in confirming participants' error detection,. However, these techniques are not well-suited for application in studies based on ADL performance due to the extensive movements made by participants during task execution. However, the development of new techniques such as functional near-infrared spectroscopy (Koehler et al., 2012; Piper et al., 2014) or portable eye-tracking equipment (*e.g.*, Tobii X2-30 eye tracker; Tobii Pro, 2014) may offer a future solution to this problem by allowing the registration of functional brain activity or capturing visual behaviour in real-world environments with no movement restrictions.

9.2.4. Steps predictability applied to activities of daily living evaluation

Another critical aspect that we have found to influence ADL monitoring and error detection is the predictability of step actions, as demonstrated by the finding of Study 3. This study revealed that different neural networks are engaged in the monitoring of highly-predictable and low-predictable steps. Highly-predictable steps are inherently linked to the preceding step and, when they occur, they confirm the observer's expectation (Alagoz et al., 2010; M. M. Botvinick & Plaut, 2006). This characteristic, together with the neural circuitry associated with these steps (including perceptual and motor areas), suggests that such events are processed quite automatically. Consequently, as also confirmed by the behavioral data in Study III, the observer can rapidly confirm the correctness of these steps.

Conversely, in the case of low-predictable steps, there is not a clear expectation regarding the next step. Therefore, additional monitoring processes are necessary to determine the correctness of these events. This differentiation might have relevant implications for the assessment of patients' ADL performance and monitoring. An evaluation based on actions predictability may reveal two distinct impairments patterns during ADL performance. Some patients may primarily make errors in low-predictable steps, while others may err even in highly-predictable steps. These two behavioral profiles may reflect different cognitive impairments. Specifically, difficulties in executing and monitoring low-predictable steps may be associated to more genuine monitoring impairments and to alterations of higher-order executive functions (*e.g.*, working memory, inhibition, etc.) (Cooper & Shallice, 2006; Cooper & Shallice, 2006; Cooper & Shallice, 2000; Forde & Humphreys, 2000). However, if a patient struggles with both types of steps, this may reveal a more deep impairment of semantic knowledge about ADL actions (Forde & Humphreys, 2000). This assessment can assist the clinician in gaining into a more comprehensive understanding of the cognitive mechanism(s) contributing to patient's online SA impairments.

9.3 Revisiting the relevance of conflict monitoring as a key process for self-awareness

Study II (Chapter 7) identifies conflict monitoring/resolution as a key component of SA, which constitutes an important piece of knowledge within the whole picture of anosognosia. In order to better understand this finding it will be discussed in the context of previous research about the role of *conflict monitoring in metacognition*.

As previously introduced in Chapter 2, the *dynamic filtering theory* proposed by Shimamura (2000) accounts for the relationship between EF, metacognition and the frontal lobe (Shimamura, 2000a, 2000b). The author proposes that the (top-down) control that the meta-level exerts on the object-level could also occur prior to the actual performance of the task. In fact, during the performance of experimental tasks a negative ERP, the "contingent negative variation" (CNV), is observed when participants receive a cue to prepare to the incoming task (Gardiner, 1911; Walter et al., 1964). The CNV represents an anticipatory control that influences the cognitive processes that are going to be implemented during the task performance (*e.g.* the increment of the processing of task-relevant dimensions or characteristics) (Shimamura, 2008; Walter et al., 1964). It has been observed that patients with dorsolateral prefrontal lesions exhibit reduced CNV and difficulty to attend the relevant dimension of stimuli (Rosahl & Knight, 1995). The author raises the possibility of this pattern being caused due to the failure of the PFC to produce the top-down preventive control on the activity of posterior processing areas (*i.e.* the object-level processing), resulting in an enhanced between-processes conflict during task performance (Shimamura, 2008). This theory can be reconnected with SA thinking on how metacognitive offline SA interacts with online performance through the anticipatory awareness component. In fact, anticipatory awareness, based on the evaluation of prior experiences with similar context demands (*i.e.* metacognitive awareness), helps us to apply the appropriate cognitive resources to deal with the present context (Crosson et al., 1989; Toglia & Kirk, 2000). Regarding the results of Study II, participants with unimpaired offline SA could have a more realistic perception of the difficulty of the task in relation to their own abilities. As a result, these participants mobilize the adequate preventive control during the *3 Conflict Cognitive Control Task*, being more prepared to monitor and solve the conflicts and being their performance less affected by the presence of the conflicts.

As an example of how this mechanism might work when performing ADL, in the *Breakfast and Dressing Conflict Task* during the anticipatory awareness assessment (*i.e.* the prediction of the performance in the incoming task), some participants, even if not required, gave an explanation about why they anticipate that some errors could be made. For example one participant anticipated some errors during the *Breakfast Task* because, she said: *"I've never used a juicer like this before; I don't know exactly how it works"*. This example reflects that the participant made an evaluation of the context and, based on her previous knowledge and experiences (*i.e.* metacognitive awareness), anticipated that she could have some problem during the task performance. In turn, this anticipation might have resulted in the participant being more cautious and implementing more attention when using the juicer. This hypothesis could be explored during the *Breakfast and Dressing Conflict Task* by asking a more detailed self-assessment from participants regarding their upcoming performance. Subsequently, an analysis would be conducted to determine if the participants who express concerns about specific conflicting situations, indicating that these situations might create a problem during performance, are also the participants who better anticipate them.

The previous arguments serve to show how offline SA could affect conflict monitoring. However, given the dynamic interaction between SA components, and based on the regression analysis of Study II, next we are going to revisit *how conflict monitoring can affect offline SA*. Quiles et al., (2020) observed that self-evaluation was related to emergent awareness in tasks that required high-level cognitive functions (*i.e.* social cognition) but not in basic-level cognitive tasks (*i.e.* memory). This pattern might be due to the fact that experimenting difficulties during the task constitutes important information for self-evaluation (Toglia & Kirk, 2000). In line with this idea, it has been observed that during the performance of experimental tasks, the presence of conflicts, not only affects task performance, but also influences metacognitive judgments (for a recent review see Questienne et al., 2021). These studies found an association between the presence of a conflict during task performance and participant's subjective feeling of control, the rating of task difficulty and the so-called urge-to-err (*i.e.* the impulse of making an error) (Desender et al., 2016; Morsella et al., 2009; Questienne et al., 2021). All these aspects might be important for the posterior self-evaluation of performance (Desender et al., 2017). Interestingly, some studies observed that not only the presence of the conflict, but also the *subjective experience* of the conflict might affect these metacognitive judgments (Desender et al., 2017, 2014). Therefore, based on the "*feeling"* of a conflict during the task, one might evaluate the task as difficult and problematic and the performance as effortful (Dunn et al., 2019) and this would be the information that is going to be integrated in the offline metacognitive knowledge. Connecting this idea with what observed in the performance of the *Breakfast and Dressing Conflict Task*, during the self-evaluation assessment (*i.e.* the rate of the performance after the completion on the task) our participants frequently referred to the conflicting situation when rating the difficulties experimented during the task. This information might then be integrated in the metacognitive knowledge and the participant is going to believe that sometimes, depending on the context, even apparently simple tasks such as preparing a breakfast might carry some difficulty and they may require behaving with some caution. Further studies are needed in order to explore this hypothesis further.

According to relevant theories, *conflict monitoring* might also have an important role in *emergent awareness* (Holroyd & Coles, 2002; Holroyd & Yeung, 2012b; Nick Yeung et al., 2004). The *conflict theory,* proposed by Yeung et al.'s (2004) in the context of experimental tasks, highlights the importance of conflict detection as an initial input that leads to error detection (Steinhauser & Yeung, 2010; Yeung & Summerfield, 2012; Yeung et al., 2004). That is, after the commission of an error, the monitoring system detects the conflict between the performed incorrect response and the correct response, manifested by the ERN. This mechanism of conflict detection is used as a signal to the system that additional information is required regarding the event. This signal leads to the subsequent accumulation of evidence, enabling accurate error detection (Wessel et al., 2011; Yeung & Summerfield, 2012). Therefore, getting back to the results of Study II, it is likely that the participants with more ability to monitor conflicts between competing responses (even before or after the response) have more chances of detecting error during the performance.

The performance of some patients during the *Breakfast and Dressing Conflict Task* could help us to understand how the mechanism of conflict detection may impact emergent awareness in everyday tasks. In the *Breakfast Task,* some errors resulting from conflicting situations led to explicit and visible feedback. If the participant assembled the juicer incorrectly, it resulted in the juice spilling over the table, clearly indicating that something had gone wrong. Interestingly, some patients recognized and verbally reported that the juice was spilling over the table, yet they took no action to correct the error and continued squeezing the orange with the juicer. One possible explanation for this behavior is that these patients objectively noticed that the juice spilling over the table was an inappropriate outcome. However, due to their failure in detecting of a conflict between their incorrect action and the correct action, they did not recognize the error as being produced by themselves. Instead, probably they attributed the outcome to an external factor rather than to their own mistake. The study of EEG evoked potentials within the context of experimental computerized tasks could provide a means to test this hypothesis by focusing on two ERP: the ERN and the Feedback-Related Negativity (FRN). While the first component reflects the neural response to errors the FRN associated with the neural response to unexpected outcomes (Hoffmann & Falkenstein, 2012; Miltner et al., 1997; Ullsperger et al., 2014). Therefore, it is possible that patients exhibiting this particular behavioral pattern during the may show affected ERN, with intact FRN (Llerena et al., 2016).

In addition, it may be beneficial to incorporate an assessment of the locus of control into the evaluation protocol for patients that exhibit this behavioural pattern (Judge et al., 2005; Rotter, 1966). This might help to understand whether they primarily attribute the wrong occurrences in their lives to external factors rather than to internal ones.

It is important to acknowledge that all these parallelisms proposed between the results of Study II and anticipatory awareness, self-regulation and behaviors with conflicting situations observed during the performance in the *Breakfast and Dressing Conflict Task* are motivated by the interest of understanding how conflict monitoring is involved in SA in daily functioning and naturalistic tasks. In addition, the fact that the findings derived from an experimental task might have applicability in explaining everyday behaviors is an important aim of Study II. However, these parallelisms are not based on formal statistical analyses and have to be considered as explicative hypothesis based on the qualitative observation of participants performance. Further research is needed to test the reliability of these hypotheses.

9.3.1. Alternative approaches to understand conflict monitoring in activities of daily living error detection

The importance of conflict monitoring for error detection is also suggested by some of the findings of Study III. A part of the omission-commission pattern previously described, the relevance of conflict monitoring for error detection is also suggested by the finding of overlapping neural activation in response to errors and low-predictable steps. Yeung & Summerfield, (2012), as an extension of the conflict theory, suggest that error detection is associated with another metacognitive process, *decision confidence*. The link between these two metacognitive processes was confirmed by the fact that the Pe, the electrophysiological marker previously associated to error detection, is also sensitive to confidence judgment in correct trials, with greater Pe amplitude being associated with more uncertainty (Yeung & Summerfield, 2012). The fact that the Pe amplitude changes as a function of confidence reveals an important aspect of error detection: error detection is not an all-or-nothing phenomenon (Boldt & Yeung, 2015; Scheffers & Coles, 2000). In fact, it could be seen as a continuous process based on response confidence. The dissociation in the neural response found for highly-predictable vs. low-predictable steps and the fact that errors elicited the same neural response as low-predictable steps are congruent with this idea. In fact, within an ADL sequence, if the action observed is not clearly correct (as in the case of high-predictable steps), a monitoring mechanism starts up to evaluate the correctness of such an action. This monitoring mechanism could be the one that finally leads to judge the action as correct or as an error.

9.4. Implications of the present studies for clinical practice

The findings reported in the present dissertation have several important implications for clinical practice. Even if nowadays SA is more frequently evaluated in clinical practice than before, usually only offline SA is taken into consideration. However the importance to assess all the components of SA has been widely highlighted throughout this dissertation. The protocol proposed in Study I might be used in clinical practice to identify which component is mostly responsible for anosognosia. This information is crucial for designing efficient and personalized rehabilitation programs that best suit to a given patient. For example, as previously stated, one of the broadly used interventions to recover SA is based on giving the patients external feedback (*i.e.* verbal feedback to errors or video-feedback; Toglia & Goverover, 2022; Villalobos, Bilbao, et al., 2020). This type of intervention might be especially useful to improve SA in patients with impaired online emergent awareness, where the detection of errors and problems during task execution is compromised (Agnew & Morris, 2010; Morris & Mograbi, 2013; Sunderaraman & Cosentino, 2017b; Toglia & Kirk, 2000). However, this type of intervention might be less effective with patients that show mnemonic anosognosia, where memory consolidation problems hinder the new experiences from being integrated into the previous metacognitive knowledge (Mograbi et al., 2009; Sunderaraman & Cosentino, 2017b). Therefore, selecting the intervention based on the specific SA component that is compromised is imperative when designing the treatment protocol for ABI patients.

In turn, empirical research is fundamental to understand which intervention is useful for which SA component. However, the majority of studies tested the efficacy of SA treatment using as the principal outcome of the intervention offline SA measures (Brown et al., 2021; Engel et al., 2019; Robertson & Schmitter-Edgecombe, 2015; Schrijnemaekers et al., 2014). Nevertheless, the exhaustive evaluation of online SA is important when investigating interventions efficacy. As an example, imagine that we want to prove the efficacy of a new treatment for ISA, specifically targeting the self-evaluation component of SA, but the pre-post intervention assessment is only based on offline SA. If we find that this treatment had no effect on improving ISA we can suppose that our new intervention is not appropriate for rehabilitating ISA at all. However, the results may be caused by the fact that the sample included in our study was characterized by impairments in other SA components (*e.g.* emergent awareness, updating). Therefore working with these patients the self-evaluation process was ineffective for ISA rehabilitation. Therefore, in this case treatment effects should be tested directly assessing pre-post changes in the self-evaluation component. To sum up, the *Breakfast and Dressing Conflict Task* constitute an evaluation tool that might be used in both clinical and research settings in order to have a more comprehensive understanding of the impaired component that underlie ISA. This information might guide intervention selection in clinical practice and help generating finer hypotheses in ISA rehabilitation research (Engel et al., 2019).

If emergent awareness is found to be affected, it is important to conduct a qualitative assessment to identify which errors the patient struggles to detect. This information is crucial for designing an individualized intervention strategy that addresses the specific altered mechanism affecting online error detection. For example, continuing with the hypotheses previously proposed (section 9.2.3), if a patient struggles to detect violation errors, the intervention may involve enhancing the activation of the correct sequence of steps. This could be achieved, for instance, by recalling the sequence before starting the task. In alignment with this approach, Bettcher et al., (2011) employed the Task Training NAT (TT-NAT), a modified version of the original NAT designed to address error detection impairments arising from compromised task knowledge. The intervention included the recalling of the required objects and the sequence of steps prior to the actual task performance. The authors reported a higher rate of detected errors in the TT-NAT compared to the Standard-NAT (Bettcher et al., 2011). However, it's worth noting that this approach may be more effective for improving the detection of violation errors, as opposed to other error types not linked to the knowledge of the sequence. For example, to enhance the detection of repetition errors, an appropriate intervention strategy could involve improving short-term memory during the task by recalling the previously executed steps. These two interventions proposed here are quite distinct and cannot be applied indistinctly to every patient that exhibit impaired online SA. In fact, each intervention targets a particular mechanism that might be implicated in error detection, and these mechanisms may be affected independently. Future studies could consider the various error types when assessing emergent awareness and examine whether error monitoring rehabilitations are effective based on the specific error type being analyzed.

Similarly, assessing error patterns based on step predictability can be essential for tailoring individualized interventions. For instance, if the error pattern indicates difficulties in monitoring low-predictable steps, the intervention should prioritize enhancing automaticity during task performance by incorporating more highly-predictable steps. According to Botvinick & Plaut (2004), around the middle of the task, there is a decline in contextual information (e.g., general task goals and previous steps), which increases the likelihood of errors, especially those related to less automatic (low-predictable) actions (Botvinick & Bylsma, 2005). Therefore, an effective strategy to address a high error rate with low-predictable steps could involve training the patient to complete steps such as adding sugar or milk to the cup at the beginning of the task. Finally, this profile of patients may be trained to pay more attention when performing low-predictable steps. On the contrary, if the patient produces a large number of errors even in highly-predictable steps this may reflect a deeper impairment in the correct semantic memory of ADL actions. This impairment might be addressed from a compensatory strategy, for example, by including cognitive intervention aimed at enhancing the sequence knowledge and sequence steps activation (Bettcher et al., 2011).

Finally, the knowledge that conflict monitoring might be a key executive component that influences ISA can be applied to design rehabilitation approach in clinical practice. As previously stated, strategies based on external feedback to errors are among the most used for ISA rehabilitation. On the other side, *experiential feedback,* that is experiencing difficulties during real-life tasks performance, has been proposed as an effective technique to improve SA (Barco 1991; Lucas and Fleming 2005). Some empirical findings suggest that experiential feedback is effective for improving online SA (Ownsworth et al., 2008; Ownsworth et al., 2010). Nevertheless other studies observed that experiential feedback may not be so effective as other forms of external feedback (Schmidt et al., 2013). However, in these studies experiential feedback missed the original assumption at the basis of this technique and the intervention was based on merely repeated practice of the task. However, the original idea of the experiential feedback is based on the necessity of experiencing some difficulties during task performance, as reflected by the fact that this technique was also referred to as "*planned failure"* (Lucas & Fleming, 2005). The results of Study II, which show the importance of conflict monitoring for SA, support the potential benefit of conflict-based experiential feedback for SA and might guide the development of new strategies to implement this technique. In fact, increasing conflict monitoring demands during task performance might be a key aspect when using experiential feedback to improve SA. Based on this idea, we recently designed in our laboratory an intervention that implements external online and video feedback strategies while the patient performs a task with increasing conflict monitoring and resolution demands (ClinicalTrials.gov_NCT03958487). The conflict monitoring demands are progressively increased by introducing a larger number of distractors and conflicting situations similar to the ones used in the *Breakfast and Dressing Conflict Task* from one session to another. Based on the results found an experimental single-case study this intervention demonstrated to be effective to improve both online SA and the ability of the patient to detect and effectively deal with completely new distracting and conflicting situations. This effect was found not only during the performance of the trained task, but also when performing an untrained task (Salazar-Frías et al. *submitted*). This intervention could be especially useful for patients with anosognosia that show conflict monitoring and resolution impairments.

9.5. Conclusions remarks

The present thesis aims to provide a deeper understanding of SA and its alterations after ABI in the context of familiar ADL. In particular, the present dissertation addresses important aspects that were still unresolved in the literature, such as the need to improve SA assessment and the understanding of specific cognitive and neural mechanisms involved in SA.

In the first study, we provided preliminary positive findings about the validity of a novel assessment tool, "The Breakfast and Dressing Conflict Task" to measure all online SA components at a time in the context of familiar and significant ADL. The relevance of this finding is threefold. On one hand, it responds to the need to develop new assessment tools sensitive to the multi-component nature of SA, in order to better identify the specific profile of SA impairment that might suffer a given ABI patient. Second, this kind of instrument, as it requires participants to perform two familiar ADL it also provide more ecological validity in the evaluation of SA. Third, the specific design of our tool, evoke specific error types, might help to simplify the SA coding system, which is typically based on spontaneous errors in most ADL-based tasks and can be very effortful and time-consuming. The finding that the Conflict Monitoring Index derived from our task based on responses towards these evoked situations also correlated with traditional measures of online SA, make our task potentially more suitable for clinical practice.

Secondly, the present thesis addresses the cognitive and neural mechanisms underlying SA with an approach based on specificity and qualitative differences. We found that *conflict monitoring* processes such as the ones typically measured in Stroop like tasks may be a specific EF mechanism especially relevant in emergent awareness. Different findings from the present dissertation support this idea. First of all in Study II we directly tested this hypothesis, with the finding that the ability to detect and solve conflict in experimental tasks was associated and predicted the ability of detecting errors (i.e. emergent awareness) in an ADL such as preparing a breakfast. This pattern of association provides preliminary evidence that a common cognitive mechanism might be involved in conflict monitoring in experimental tasks and monitoring errors in everyday situations. Additionally, the findings of Study III that different cerebral networks respond to omission and commission errors and the fact that unpredictable (or conflicting steps) and erroneous steps show overlapping neural activation may represent supplementary neural evidence of the relationship between conflict monitoring and error detection.

Furthermore, the results of this thesis show the importance to use a qualitative approach when studying SA awareness and its components in both research and clinical settings. In line with this, in Study I we encountered that the various online SA components behaved differently depending on the task performed (BADL or IADL). Different patterns of associations were found in each task between the online SA components and the offline SA and sociodemographic, neuropsychological and clinical variables. This suggests the importance of including different types of tasks when assessing SA. In addition, the finding of neural qualitative differences between errors types (*i.e.* omissions, repetitions and violations) and between different types of steps (*i.e.* high-predictable vs. low-unpredictable) also suggests that these aspects should be taken into account to have a more comprehensive understanding of patients' monitoring deficits. This qualitative evaluation is important source of information that might guide the selection of appropriate rehabilitation strategies.

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