Fostering advances to neuropsychological assessment based on the Research Domain Criteria: The bridge between cognitive functioning and physiology

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ABSTRACT

Objectives: The current review aimed to explore the advances in neuropsychological assessment in light of a recent research framework designed to improve our knowledge on mental health – the Research Domain Criteria (RDoC).

Methods: RDoC proposals on neuropsychological tests were reviewed across the RDoC cognitive systems domain. The focus is on the physiological unit of analysis and the potential applications are illustrated given the functional relevance of RDoC constructs to psychopathological and neurological conditions.

Results: The advances in neuropsychology anchored in RDoC are not observable in terms of innovative paradigms, but rather in the neurobiological correlates that may be obtained from the classical neuropsychological tasks. The behavior unit of analysis may be integrated with physiological outcomes while mapping distinct cognitive constructs simultaneously.

Conclusions: Under the aegis of RDoC, the integration of multiple levels of analysis allows to obtain a more detailed and complete neuropsychological characterization with high potential to be translated into better intervention strategies.

Introduction

According to Reinvang (1999), the field of neuropsychology remained as the only method for investigating the living human brain and its relation to cognition until the 1960s. Since then, accelerated progresses and innovative ways to approach neuropsychology have been observed.

Today, clinical neuropsychology is considered a psychology specialty dedicated to promote a deeper understanding of the relations between the brain and behavior, based on the study of the central nervous system and its relation to human behavior.

This knowledge can be applied in the assessment and diagnosis of neurocognitive-related disorders and contribute to the improvement of treatment and rehabilitation (American Psychological Association, 2010).

However, it is unclear whether the advances in neuroscientific knowledge informed current methods of neuropsychological testing and assessment. Recently, the Research Domain Criteria (RDoC), an initiative from the National Institute of Mental Health, emerged as a research framework that aims to improve the understanding of mental processes. The RDoC matrix (see https://www.nimh.nih.gov/research-priorities/rdoc/constructs/rdoc-matrix.shtml) is the core of RDoC and describes basic biopsychological processes (domains of functioning and constructs) and their respective observable manifestations (units of analysis) (Cuthbert & Insel, 2013; Kozak & Cuthbert, 2016). Each construct represents a specific dimension within five domains of functioning – Negative Valence Systems, Positive Valence Systems, Cognitive Systems, Social Processes, and Arousal and Regulatory Systems – and reflects basic brain mechanisms that are transdiagnostic in nature, that is, that are not bounded by the current taxonomic models of psychopathology. The Cognitive Systems are particularly relevant to neuropsychology since its constructs – attention, perception (visual and auditory), declarative memory, language, cognitive control (updating, inhibition, performance monitoring), and working memory (WM) – intersect with the common practices of neuropsychological assessment and rehabilitation. The RDoC matrix provides a research framework based on units of analysis that allow measuring the mentioned constructs at the molecular, cellular, circuit, physiological, behavioral, and self-report levels. Several classical neuropsychological tasks are presented in the RDoC matrix to cross and accommodate findings between different levels of analysis.

Neuropsychology is dedicated to isolate brain-performance correlates using behavioral data (Reinvang, 1999; Walhovd & Fjell, 2003). Behavioral approaches to cognition rely on performance speed and accuracy that are assumed to reflect the functioning of the brain processing system (Walhovd & Fjell, 2003). Nevertheless, the integration of indicators that reflect distinct aspects of brain functioning may advance our knowledge on neuropsychological assessment (Reinvang, 1999; Walhovd & Fjell, 2003). Cognitive processes may be detected by (neuro)physiological indicators while disentangling perceptual, cognitive, and motor contributions to speed and accuracy (Walhovd & Fjell, 2003). In this line, RDoC offers a promising venue to map relevant brain processes in terms of behavior and physiology. That is, the RDoC framework may add information to the current behavioral indices and provide a neuroscience-based approach to foster advances in neuropsychological assessment and rehabilitation.

To the RDoC cognitive system domain and physiology, electroencephalogram (EEG) is the primary method for assessing temporally precise neuronal processes (Maguire & Abel, 2013), particularly in the time and frequency domains. Along with neuroimaging, these techniques are of high importance to unveil the neuropsychological substrates of behavior. Cognitive event-related potentials (ERP) are online processing measures that have interesting possibilities to clinical neuropsychologists. The accumulated research on ERP in the last decades provides useful insights to study processes of central interest to neuropsychology, namely the neuronal underpinnings of cognitive functions. Brain ERPs may be obtained from tasks that are comprised in classical and widely used neuropsychological tests and may be useful to individual assessment

(Reinvang, 1999). In fact, ERPs show good psychometric properties in test–retest reliability and internal consistency, particularly in what concerns amplitude measures (Clayson & Larson, 2013; Meyer, Bress, & Proudfit, 2014; Reinvang, 1999; Rietdijk, Franken, & Thurik, 2014). The millisecond time resolution of ERP analysis allows tracking the sequence of neural engagement elicited by specific brain processes. Therefore, it is possible to map brain processes since early stages of perception attention, until further and more complex cognitive functions.

To understand how brain regions communicate, it is also crucial to underscore the dynamics of brain processing (Bonnefond, Kastner, & Jensen, 2017). Magnitude changes in frequencies quantify neural oscillations and provide a reliable index of brain resources allocated to experimental tasks (Bonnefond et al., 2008). Consistently, the oscillatory analysis is included into the RDoC matrix. Magnitude oscillations occur when the amplitude of certain frequency power bands increases in response to a stimulus (Maguire & Abel, 2013). The change in amplitude manifests the activation of additional neural assemblies firing at the same frequency (neuronal synchrony). Generally, the oscillations rely on the conventional clinical frequencies, distinguishing between the delta, theta, alpha, beta, and gamma waves. Compared to ERPs, the changes detected in neural oscillations reflect more directly the inter-neuronal communication and are sensitive to different properties of brain functioning, providing additional and complementary information to ERPs (Maguire & Abel, 2013). The main assumption is that different neural assemblies are involved in different cognitive processes, generating oscillations in distinct frequency bands (Yeung, Han, Sze, & Chan, 2016). These dynamic oscillations unveil neuropsychological processes, with some studies reporting correlations between performance and frequency activation (e.g. Yeung et al., 2016). Abnormal oscillations may be, then, indicative of abnormal brain activations.

In the recent years, changes in neuropsychological practices have been promoting a deeper understanding of the cognitive functioning through a greater sophistication of the assessment process (Casaletto & Heaton, 2017; Groth-Marnat, 2003). This is partly due to the introduction of novel standardized instruments, with new methodologies, and the focus on new outcomes (such as functionality and quality of life). Despite that the classical tasks are largely used in the neuropsychological practice because of the well-established validity and discriminative power of these instruments. A recent review on the advancements of neuropsychological assessment (Casaletto & Heaton, 2017) highlighted the importance of increasing the early detection of brain changes by merging neuropsychological assessment instruments with multimodal markers of neurological functions, which could improve our knowledge and comprehension of brain–behavior relationships.

Accordingly, the current review aims to explore whether RDoC proposals may foster advances in neuropsychological assessment, by incorporating new methods on classical assessment tasks. The focus will be on RDoC Cognitive Systems domain, considering the critical role that the gold standard tasks of neuropsychology play in the RDoC matrix to assess attention, visual and auditory perception, declarative memory, language, cognitive control, and WM. For each construct, widely used neuropsychological tasks in practice were selected by experts on this area. It was also considered the potential of the instruments to be adapted to computerized versions, as physiological data may be obtained from these versions when synchronized with EEG. This allows obtaining both behavioral measures and its neurophysiological correlates. The integration of multiple levels of analysis may allow to obtain a more detailed neuropsychological profile. Despite recognizing that further neurophysiological correlates can be of value for the analysis of cognitive functioning, we focused only on the neurophysiological correlates contemplated in the current version RDoC matrix. Finally, and for each construct, neurological or psychopathological conditions will be reviewed to describe advances in the field. Despite the fact that RDoC does not recognize *a priori* diagnoses (Cuthbert & Insel, 2013), it is possible to illustrate the applications of the RDoC matrix to clinical findings from the existing literature, given the functional relevance of its constructs to psychopathological and neurological conditions.

RDoC attention construct

Definition

The first construct of cognitive systems described in the RDoC matrix refers to the attentional processes that regulate the access to capacity-limited systems (e.g. awareness, perceptual processes, motor action). Attention is, then, the ability of information processing, which is limited and often intentionally controlled (Styles, 2006). The concepts of capacity limitation and competition are inherently associated to selective and divided attention.

Measurement paradigm

In this regard, dual-task paradigms have been widely used in (neuro)psychology since the late 19th century to measure the divided attention between two qualitatively different tasks. Such paradigms require the participants to perform two tasks simultaneously. Normal subjects show a deterioration in the performance of the dual task (the decrement effect), compared with when both tasks are performed separately (Luck, 1998). The rationale of the dual-task asserts that to investigate how attentional resources are allocated the patterns of interference should be examined while overloading the processing system (Kok, 1997). The attentional resources allocated to the processing of stimuli in the secondary task will decrease in function of the priority given to the primary task.

The interference elicited by dual-task demands has been studied for several decades (Luck, 1998). The typical indicators of interference in dual-task performance are prolonged reaction or response times and increased error rates.

Neurophysiological correlates

From the accumulated knowledge on attentional processes in dual-task paradigms, the neuroscience efforts were redirected to isolate the neurobiological correlates of divided attention. Empirical studies systematically evidenced that the P3 ERP has a modulatory and a functional relevance coherent with the dual-task decrement effect (Kok, 1997). In this line, P3 was integrated in the RDoC matrix as a physiological index of divided attention.

The P3 component is a positive electrophysiological response that peaks around 300 ms post-stimulus onset, namely for auditory stimuli (Luck, 2005). Both P3 amplitude and latency are sensitive to the amount of attentional resources allocated (Polich, 2007) and is accompanied by a set of short-lived co-occurring psychophysiological changes, as pupil's dilation (Nieuwenhuis, De Geus, & Aston-Jones, 2011). The amplitude of the P3 wave is decreased and the latency is delayed when perceptual processing resources are diverted away from the P3-eliciting stimuli in dual-task experiments.

In Wickens, Isreal, and Donchin's (1977) seminal study, participants were asked to manipulate a control stick to keep a randomly moving cursor on the display centered with the target while counting deviant stimuli during an auditory oddball task. As expected, P3 amplitude in the secondary task decreased compared to the single-task condition. A posterior study replicated these results, showing that P3 amplitude was reduced when tones were counted in concurrence with visual tracking (Isreal, Chesney, Wickens, & Donchin, 1980).

The main findings highlight that the single- and dual-task conditions share some perceptual-central resources (Kok, 1997). Subsequently, when high cognitive resources are elicited by the dual-task demands, this will limit the amount of available attentional resources, as measured by reduced P3 amplitude and longer latencies (Polich, 2007). The dual-task decrement effect is, therefore, observable in P3 modulation. Several authors documented this reduction in P3 amplitude (e.g. Isreal et al., 1980; Luck, 1998; Polich, 2007; Singhal, Doerfling, & Fowler, 2002; Wickens et al., 1977), but not in early potentials, suggesting that the interference occurs at a late stage of processing. Such reductions were not separately observed in N1 and P2 amplitude as a result of the introduction of the dual task (Kok, 1997; Luck, 1998; Singhal et al., 2002), reflecting an effect on the N100–P200 complex as a whole (Singhal et al., 2002). Moreover, the N1–P2 complex seems to reflect an automatic gating mechanism sensitive to the load imposed by both tasks, not related to divided attention. Thus, the participants were initially able to identify the secondary stimuli without any interference but some interference was present at a later stage as evidenced by suppressed P3 amplitude (Kok, 1997; Luck, 1998).

From the empirical evidence systematically suggesting differential P3 modulation during single- and dual-task conditions, RDoC proposed P3 as a neurobiological index of divided attention.

Clinical findings

Deficits on divided attention – as captured by P3 modulation – show interesting possibilities and applications to neuropsychological research and assessment. The P3 is considered an index of executive functioning (Perry & Hodges, 1999). Short P3 latencies and high amplitudes are consistently associated with improved executive functioning. The role of executive attention in complex tasks is often addressed in clinical neuropsychological assessment and P3 may provide an independent physiological measure of attention. For example, the P3 decrement effect in Alzheimer disease (AD) would allow examining whether slowed processing or greater interference between stimuli explains the poor performance in dual tasks (Perry & Hodges, 1999).

Recently, Parra, Ascencio, Urquina, Manes, and Ibanez (2012) investigated whether the P3 allows to identify the risk for the AD at early stages, based on the assumption that mild cognitive impairment is a subclinical form of dementia that progressively impairs attention and, subsequently, memory control. The combined use of sensitive neuropsychological tasks and the analysis of P3 modulation may work together as a useful method for the subclinical assessment of Alzheimer. In addition, P3 modulation is relatively independent from confounding variables that may affect behavioral measures (Parra et al., 2012; Walhovd & Fjell, 2003).

RDoC perception construct

Definition

According to RDoC, perception may be understood as a set of mandatory processes to perform computations on sensory data, by acquiring new information from the external environment, as well as by transforming representations and make predictions of the external context. In particular, visual and auditory perception are of high interest to the neuropsychological field.

RDoC visual perception subconstruct

Definition

Visual perception regards the ability to perceive the surrounding environment through vision, allowing to organize and interpret visual information (Wade & Swanston, 2001). Due to the high number of visual stimuli in our daily life, RDoC presents a wide range of paradigms targeting different processes of visual perception, such as face identification, figure ground, and identification of emotion expressions.

Measurement paradigm

Our focus will be on identification of emotion expressions, due to its central role in visual perception and in several daily activities, namely cognitive control, behavior monitoring, and decision-making (Inzlicht, Bartholow, & Hirsh, 2015; Sorce, Emde, Campos, & Klinnert, 1985). From the functional perspective, emotions comprise physiological, behavioral, cognitive, and affective processes that promote automatic and adaptive responses to the environment (Shariff & Tracy, 2011). The paradigms for the identification of emotion expressions require the participant to identify facial expressions of emotion through the visualization of a set of photographs that are being developed since Ekman's work in the 1960s (Ekman, 1992).

Neurophysiological correlates

Variations in EEG frequency bands may be a critical tool to analyze the cognitive processes related to emotional phenomena (Aftanas, Varlamov, Pavlov, Makhnev, & Reva, 2002; Balconi & Lucchiari, 2007; Balconi & Pozzoli, 2009). Specifically, alpha waves are neural oscillations in the frequency range of 8–13 Hz that seem to be associated with emotional identification (Harmon-Jones, 2003). Considering the wide use of emotion identification tasks, both in traditional neuropsychological instruments and in experimental paradigms, alpha activity may be considered a neurobiological correlate of visual perception (Klimesch, Fellinger, & Freunberger, 2011). Alpha power is inversely correlated with regional cortical activity during task performance (Coan & Allen, 2004; Cook, O'Hara, Uijtdehaage, Mandelkern, & Leuchter, 1998; Davidson, Chapman, Chapman, & Henriques, 1990), with decreased alpha amplitudes being associated with improvements in subjects' performance and, consequently, in visual stimuli processing (Klimesch et al., 2011). Additionally, alpha activity is associated with emotional states and responses (Coan & Allen, 2004), which can provide to clinicians an opportunity to access to emotional states that are not self-reported, and to consider the involvement of emotions in subjects' performance on neuropsychological instruments.

Additionally, the high temporal resolution ERPs make them useful to differentiate between early perceptual impairments and later cognitive impairments. The visual N170 is a negative component deflection peaking about 170 ms after the presentation of a facial expression of emotion (Luck, 2005). Despite inconsistencies in the literature regarding the source of N170, some authors localized the N170 component in the fusiform gyrus. In fact, functional magnetic resonance imaging (fMRI) studies implicate the fusiform gyrus in the identification of faces (Kropotov, 2016). More consistent, however, is the finding that N170 is right-lateralized and sensitive to faces (Bentin, Allison, Puce, Perez, & McCarthy, 1996). The "face effect" in visual perception reflects increased N170 amplitude for faces, compared to non-face stimuli. Furthermore, inverted faces elicit N170 delayed latencies in comparison to upright faces, pointing to the difficulty in recognizing inverted faces (Kropotov, 2016). A reduced N170 may be, therefore, conceptualized as an electrophysiological marker of basic visual processing deficits (Maurage et al., 2007) with implications to emotion identification.

Clinical findings

In prosopagnosia – a neuropsychological condition in which individuals are unable to recognize faces – the study of N170 modulation is of great importance. Individuals with prosopagnosia show similar N170 amplitudes for faces and random noise stimuli, suggesting an attenuated sensitivity to facial expressions (Németh, Zimmer, Schweinberger, Vakli, & Kovács, 2014). As this deficit occurred in the N170 time-window, it is proposed an early visual perception deficit while detecting faces. Moreover, autism predicts N170 delayed latencies when processing visual stimuli, but the effect is not face-specific (Hileman, Henderson, Mundy, Newell, & Jaime, 2011). The same authors (Hileman et al., 2011) advanced that the reduced connectivity during the processing of complex information may explain the longer latencies. Interestingly, more negative N170 amplitudes were associated with fewer atypical social behaviors, suggesting that basic processes reflecting inefficient neural processing may translate in social interactions.

RDoC auditory perception subconstruct

Definition

Auditory perception can be defined as the ability to receive information through the auditory system and to organize and interpret it. It allows the discrimination of the various sound features and, consequently, the distinction between two successive sounds that differs in one of those features (Eggermont & Ponton, 2002).

Measurement paradigm

The oddball task consists on the interruption of a sequential presentation of repetitive stimuli by a deviant stimulus that occurs in reduced probabilities. In the auditory version, the repetitive-standard tone (usually, 500 Hz, probability 80%) is presented along with a distractive-rare one (usually, 1500 Hz, probability 20%).

Neurophysiological correlates

The mismatch negative (MMN) is a negative component that may be computed by subtracting the ERP to standard tones from the response to rare tones (Garrido, Kilner, Stephan, & Friston, 2009). Therefore, MMN is considered a robust brain response to violations of a pre-established sequence of sensory stimuli. The MMN reflects the brain's ability to perform automatic comparisons between consecutive stimuli and provides an electrophysiological index of perceptual accuracy. Garrido et al. (2009) assert that MMN is relevant to assess deficits in auditory perception that occur prior to conscious perception, with the potential to provide a reliable and stable perceptual accuracy.

As previously mentioned, the P3 component is related to the detection of novel or deviant events and to the allocation of attentional resources to that events, even in the absence of an explicit detection task (Pasion, Fernandes, Pereira, & Barbosa, 2017; Polich, 2007). The attention-orienting responses (P3a) are elicited from new sensory inputs that require an initial top-down process and are associated with a frontocentral activation (Polich, 2007). The shift of attention toward a significant event is conceptualized as a "what-is-it" detector of new, unexpected, or unpredictable events (Friedman, Cycowicz, & Gaeta, 2001). The P3a is commonly measured in three-stimuli oddball paradigms that include frequent, rare, and novel stimuli (Pasion et al., 2017), with its amplitude being higher for the former (Polich, 2007). The attention-capturing stimuli will be then represented in memory (P3b) (Pasion et al., 2017; Polich, 2007). The P3b peaks 60–80 ms later than the P3a and is considered a measure of the neural underpinnings of cognition, acting as a mismatch detector of events that do not correspond to those represented in the WM schema (Friedman et al., 2001; Luck, 2005; Pasion et al., 2017; Polich, 2007). The P3b reflects, therefore, the auditory perception of the rare stimuli.

Clinical findings

An oddball task was recently used in a study using the RDoC matrix to identify distinct psychosis biotypes using brain-based biomarkers (Clementz et al., 2015). The physiological indexes recorded in the ERP domain during the oddball task relied on the statistically derived construct of sensorimotor reactivity. This reactivity had a prominent role in describing neurobiological deviations in psychosis, allowing to distinguish between biotypes. The more severe expressions of psychosis (biotypes 1 and 2) were characterized by a dysfunction in the reactivity to the sensory events of the oddball task, which may compromise the discerning of environmental stimuli relevance. Previous meta-analytic studies have documented that MMN (Umbricht & Krljes, 2005) and P3 amplitude (Jeon & Polich, 2003) are significantly reduced in patients with schizophrenia. Umbricht and Krljes (2005) propose that the impairment in the auditory sensory reactivity and context-dependent information processing not only include deficient performance in classical neuropsychological tasks but also extend to early steps in auditory cortical information processing. In the meta-analyses of P3 modulation effects, the results were more robust for the auditory oddball ($d = 0.89$) than other tasks. In line with RDoC proposals, P3 obtained from oddball paradigms may be a robust biological marker for schizophrenia as indexing disturbances in attentional allocation mechanisms.

RDoC declarative memory construct

Definition

As defined by the RDoC, declarative memory is the capacity to acquire, encode, store, consolidate, and retrieve representations of facts and events. Declarative memory underlies relational representations, facilitating the recall of new information. It can be subdivided in two major categories: (a) episodic memory, comprising contextual relations among items and providing cues to the representation of events; and (b) semantic memory, facilitating the integration and organization of the factual knowledge. Furthermore, scientific findings are reporting autobiographical memory as one important feature of declarative memory, respecting to the conscious recollection of personally relevant events, which integrates both episodic and semantic memory (Cabeza & St Jacques, 2007; Conway & Pleydell-Pearce, 2000).

Measurement paradigms

Declarative memory has a significant impact on the daily life of the individuals, due to the importance of being able to recall facts and events on the identity formation and integrity. Considering this impact, memory function is commonly assessed in the clinical practice on neuropsychology with different neuropsychological instruments, such as tasks from the Wechsler Memory Scale (Wechsler, 1997a) and Rey–Osterrieth complex figure test (Rey, 1999). Delayed recall tasks, in which persons are asked to maintain a set of stimuli online to latter reproduce it, are often used in neuropsychological assessment, either as single tests or as a part of other instruments.

Neurophysiological correlates

Neurophysiological correlates of memory show that neural oscillations of various frequency bands are associated with mnesic processes, such as encoding and retrieval information (Engel, Fries, & Singer, 2001; Jensen, Kaiser, & Lachaux, 2007). A study focused on the role of theta, gamma, and alpha oscillations in semantic and episodic memory using a face recognition task (Zion-Golumbic, Kutas, & Bentin, 2009) has reported that the formation of episodic memory is facilitated by pre-existing semantic information. Zion-Golumbic et al. (2009) have linked frontal theta synchronization and occipital alpha desynchronization to pure episodic memory processes that rely on semantic information only when it is necessary for improving task performance. Gamma waves, on the contrary, are related with pre-existing neural associations that are activated by a visual stimulus, relying strongly on semantic memory. In fact, the authors suggest that the analysis of frequency bands can provide relevant information to understand the complex relations between the neural processes underlying semantic and episodic memory, which is in line with the physiological constructs suggested by RDoC matrix. Additionally, the fact that several studies have reported a deficit in declarative memory in patients with ischemic lesions in the thalamic structures (Graff-Radford, Tranel, van Hoesen & Brandt, 1990; Malamut, Graff-Radford, Chawluk, & Cur, 1992; Nichelli, Bahmanian-Behbahani, Gentilini & Vecchi, 1988; Pepin & Auray-Pepin, 1993; Speedie & Heilman, 1982; Teuber, Milner & Vaughan, 1968) clarifies the clinical relevance of understanding the connection between semantic and episodic memory. Considering the overlaps of both processes, it can be extremely difficult to dissociate semantic and episodic memory through neuropsychological instruments. This process may be facilitated by the integration of physiological correlates.

Clinical findings

AD is one of the clinical conditions in which memory functions are most affected. Patients with AD have "forgetfulness deficit" that evolves faster than any other memory trait, regardless of the cognitive processes involved (Perri, Fadda, Caltagirone, & Carlesimo, 2013). Bobinski et al. (1995) have reported medial temporal lobe atrophy as one of the earliest markers of AD, highlighting the importance of using neurophysiological measures in early diagnosis and intervention. In what concerns to band oscillations, early markers of Alzheimer are increased theta activity and decreased beta activity, prior to a decrease in alpha activity and an increase in delta frequency (Prinz & Vitiello, 1989; Soininen & Riekkinen, 1992). A study that examined the memory-related EEG power and coherence in Alzheimer did not found significant differences in the behavioral performance of patients with mild Alzheimer compared to controls, but differences in alpha power in the temporal cortex were found (Hogan, Swanwick, Kaiser, Rowan, & Lawlor, 2003). This finding suggests that alpha power may constitute an important marker for early diagnosis of AD.

RDoC language construct

Definition

Language is conceptualized by RDoC as a system of shared symbolic representations of the world, the self, and abstract concepts that underlie thought and communication. The production of language is a complex neural process and, therefore, challenging to time-locked analysis.

Measurement paradigms

The assessment through experimental tasks, as naming tasks and detection and classification of semantic relationships, is widely used in neuropsychological assessment and allows the comprehension of language deficits. The potential of the ERPs studies using these paradigms is reported in the literature as aligned with the neural processes involved in language processing (e.g. Blackford, Holcomb, Grainger & Kuperberg, 2012; Llorens, Trébuchon, Riès, Liégeois-Chauvel, & Alario, 2014; Strijkers, Costa, & Thierry, 2010).

Neurophysiological correlates

N400 is generally thought to index the effort dedicated to lexico-semantic processing in relation to semantic memory retrieval such that words that are primed by the preceding context (words, sentences, or pictures) exhibit smaller responses than incongruous words (Kutas & Hillyard, 1980; Luck, 2005; Maguire & Abel, 2013). N400 is widely accepted as a sensitive measure of changes in language processing in participants with organic language deficits and is typically proceeded by the P600 component. P600 modulation captures continued-secondary analysis or reanalysis, often in response to conflict among levels of representation (Friederici, 2002; Luck, 2005).

Clinical findings

Aphasia is an acquired language disorder that affects linguistic domains, including speech, comprehension, reading, and writing (Ivanova, Dragoy, Kuptsova, Ulicheva, & Laurinavichyute, 2015; Wiener, Conner, & Obler, 2004), interrupting the access to language representations (McNeil, Odell, & Tseng, 1991). Abnormal N400 modulation is found in patients with aphasia (Kawohl et al., 2010; Kitade, Enai, Sei, & Morita, 1999). For this reason, Marchand, D'Arcy, and Connolly (2002) developed a computerized version of the Peabody Picture Vocabulary Test-Revised to find ERP parameters capable of maximize the correlation with behavioral performance on neuropsychological tests. In the computerized version, the pictures were presented followed by a congruent or incongruent word. A multicollinear relationship was found between N400 and performance in a sample of stroke patients (D'Arcy et al., 2003; Marchand et al., 2002). The authors concluded that N400 provides an accurate assessment of performance as that obtained from the traditional administrations forms.

Interestingly, the clinical value of N400 is also reported in children with language disorders. Despite similar behavioral performance between experimental and control groups in identifying semantically correct and incorrect words, N400 lacked the expected semantic effect in children with specific language impairment (Sabisch, Hahne, Glass, von Suchodoletz, & Friederici, 2006) and with primary language disorder (Popescu, Fey, Lewine, Finestack, & Popescu, 2009). That is, the N400 was larger to congruent conditions in the experimental groups, indicating high semantic demands even when presented with congruous words. Ors et al. (2001) found a similar non-effect among fathers of children with specific language impairment, indicating that N400 remains a residual marker of past language deficits. After completion of a language intervention program, children primary language disorder showed significant changes in N400 modulation (Popescu et al., 2009). The typical incongruent–congruent semantic effect emerged from a reduction in N400 amplitude to congruous words.

In what concerns to N400–P600 modulation, studies report distinct patterns for patients with semantic primary progressive aphasia with agrammatic primary progressive aphasia. The first group do not exhibit a N400 to semantic violations (Hurley et al., 2009, Hurley, Paller, Rogalski, & Mesulam, 2012). In contrast, when task demands to detect syntactic violations (e.g. subject-verb agreement) P600 is abnormal in aphasic patients with grammatical impairments in a great extent than N400 (Barbieri et al., 2016; Kielar, Meltzer-Asscher, & Thompson, 2012). The syntactic re-analysis is, therefore, specifically impaired in agrammatic primary progressive aphasia.

Overall, these data suggest that N400 and P600 are interesting indexes of specific processes underlying language processing deficits.

RDoC cognitive control construct

Definition

Cognitive Control is integrated into a system that modulates the goal-directed behavior based on performance monitoring. In this line, control processes are engaged in the selection of appropriate responses among competing alternatives (goal selection). Additionally, prepotent responses that are not adequate to meet the demands of the context are suppressed (inhibitory control).

RDoC goal selection, updating, representation, and maintenance subconstruct

Definition

Despite the diversity of subconstructs of cognitive control, they are somehow closely linked to each other and work together. Updating function is, normally, goal-directed. It requires the person to encode, maintain, monitor, and update the information that is relevant to that goal (Miyake et al., 2000).

Measurement paradigms

Neuropsychological instruments, such as the Wisconsin Card Sorting Test (WCST; Heaton, Chelune, Talley, Kay, & Curtiss, 1993) and the Trail Making Test (Jarvis & Barth, 1984), are extensively used in neuropsychological assessment to measure different aspects of cognitive control (Greve et al., 2002; von Bastian & Druey, 2017) related to goal selection, updating, representation and maintenance, and indexing cognitive flexibility.

Task-switching paradigms are widely used in the assessment of cognitive flexibility in experimental neuropsychology. These paradigms require the participants to switch between different cognitive tasks depending on changing rules (Allport, Styles, & Hsieh, 1994; Rogers, & Monsell, 1995). The recruitment of non-relevant cognitive processes is reduced in task-switching paradigms, as opposed to traditional tasks as the WCST (Lange, Seer, & Kopp, 2017). Processes elicited in these paradigms are, therefore, closer attributes of cognitive flexibility.

Neurophysiological correlates

Significant relations between gamma-wave responses and sensory and higher cognitive processes have been reported in several studies (Fries, Reynolds, Rorie, & Desimone, 2001; Miltner, Braun, Arnold, Witte, & Taub, 1999; Tallon-Baudry & Bertrand, 1999). Previous findings (Sederberg et al., 2007; Tallon-Baudry Bertrand, Peronnet, & Pernier, 1998) suggest that gamma oscillations might support some connections between pre-frontal cortical circuits to enhance cognitive control processes (Cho, Konecky, & Carter, 2006).

Gamma oscillatory activity cover frequencies from 30 to 200 Hz, making it possible to influence different rhythms. Due to its wide frequency range, gamma oscillations have been related to different cognitive functions and linked with information integration across various neural networks (Light et al., 2006; Uhlhaas, Haenschel, Nikolić, & Singer, 2008).

Clinical findings

Impairments in cognitive flexibility are commonly associated with aging (Berry et al., 2016), as well as psychiatric and neurological disorders, such as schizophrenia, acquired brain injury, frontotemporal dementia, and Parkinson's disease (Baez et al., 2017; Cho et al., 2006; Lange et al., 2016; Whiting, Deane, Simpson, McLeod, & Ciarrochi, 2017). This highlights the relevance of studying the neural correlates underlying this cognitive function.

A study on schizophrenia (Cho et al., 2006) reported that cognitive control was positively associated with prefrontal gamma activity in healthy controls. Importantly, the increased gamma activity was positively correlated with subjects' behavioral performance. In fact, several studies reported positive and negative correlations between gamma activity and behavioral performance in cognitive tasks (Gruber, Giabbiconi, Trujillo-Barreto, & Müller, 2006). On the other hand, schizophrenia patients have shown diminished modulation of prefrontal gamma activity (Cho et al., 2006). Gamma desynchronization was, therefore, correlated with behavioral-disorganization symptoms of schizophrenia.

RDoC response selection and inhibition subconstruct

Definition

Inhibition is defined as the ability to intentionally inhibit dominant, automatic, and prepotent responses (Isquith, Goia, & Espy, 2004; Miyake et al., 2000). It is systematically integrated into neuropsychological assessment, given the influence of inhibition on the development and functioning of other executive domains and its contribute to adaptive behavior (Huster, Plis, Lavallee, Calhoun, & Herrmann, 2014; Isquith et al., 2004; Vecchio et al., 2014).

Measurement paradigms

Stop-signal reaction time and go/no-go paradigms are widely used for assessing and exploring the underlying inhibition mechanisms (Miyake et al., 2000; Wöstman et al., 2013).

In the stop-signal tasks, participants are required to inhibit a motor response when a stop-signal appears randomly (Logan, Cowan, & Davis, 1984). On the other hand, the go/no-go paradigms require to respond to a go stimulus and to inhibit the response when a no-go stimulus is presented (van der Meere, Stemerdink, & Gunning, 1995).

Neurophysiological correlates

Providing support for RDoC proposals, alpha-band oscillation is consistently considered a neurophysiological outcome related to the performance on inhibition tasks and no-go stimuli (Babiloni et al., 2004; Bonnefond et al., 2008; Ellis, Kinzel, Salgari, & Loo, 2017; Filipović, Jahanshahi, & Rothweel, 2001; O'Connell et al., 2008; Vecchio et al., 2014; Wacker, Chavanon, Leue, & Steemler, 2010). Alpha-band oscillations have a significant role on inhibition, underlying the appropriate response selection and suppression (Klimesch, 1999; Klimesch, 2012). During the task performance, event-related alpha synchronization is positively associated with the inhibition of inadequate responses. In turn, event-related alpha desynchronization is associated with the lack of inhibitory control. Increased alpha power predicts, therefore, the high inhibitory-cognitive processes elicited by the task. (Bonnefond et al., 2008).

Clinical findings

Frontal alpha asymmetry is being reported as a possible specific biomarker of cognitive inhibition that is connected with psychological traits and conditions, as anxiety, depression, bipolarity, and hyperactivity (Ellis et al., 2017; Harmon-Jones et al., 2002; Harmon-Jones, Gable, & Peterson, 2010; Wacker et al., 2010). These studies unveil the relevance of alpha-band activity to a better understanding of psychological symptoms in neuropsychology. Alpha-band is also sensitive to age-related cognitive changes. An increase in alpha power was restricted to the younger group during a simple go/no-go while this increase was observed in older adults during a more complex version of the task (Bonnefond et al., 2008).

The authors suggested that oscillations in alpha band are sensitive to fatigue and engagement effects, demonstrating correlations with subjective evaluations. This may improve the ecological validity of neuropsychological testing by considering external factors that might influence the person's performance on behavioral measures.

RDoC performance monitoring subconstruct

Definition

Performance monitoring can be understood as the ability to monitor and adjust the ongoing performance. It is essential to the adaptive engagement in daily tasks (Larson & Clayson, 2011), once it allows to identify and solve potential conflicts that appear during the execution of a given task (Larson, Clayson, & Clawson, 2014).

Measurement paradigms

Neuropsychological traditional tests, as the Stroop Color and Word Test (Stroop, 1935), are still commonly used to assess the effect of cognitive interference in the performance (Scarpina & Tagini, 2017).

During the Stroop tasks, the participant is asked to read as fast as possible three different lists, in which two are congruent conditions and one is an incongruent one. The congruent conditions require to read the colors written in black and, then, name the color. In the subsequent incongruent condition, the Stroop effect may be detected. The participant should name the color in which the word is written, instead of reading the word (Stroop, 1935). The interference of the word with the color naming generally leads to the increase in response time and errors on the incongruent condition. Different adaptations of Stroop (e.g. auditory, emotional, and spatial versions) are frequently used as experimental paradigms to study the neural correlates of performance monitoring (Yu, Wang, Ma, Li, & Li, 2015).

For the same purpose, adaptations of the Eriksen Flanker Task (Eriksen & Eriksen, 1974) are used in experimental studies. In the Flanker task, the participants are asked to attend to and answer accordingly to the central target stimuli while it is flanked by non-distracting (congruent condition) or distracting (incongruent condition) stimulus.

Neurophysiological correlates

The relationships between performance monitoring and ERPs elicited by Stroop and Flanker paradigms are extensively studied (Danielmeier, Wessel, Steinhauser, & Ullsperger, 2009; Larson & Clayson, 2011; West, 2004) and are described in the RDoC matrix as the main physiological correlates of performance monitoring.

The error-related negativity (ERN) is a negative wave deflection that occurs before the commission of an error, peaking about 50–100 ms after an erroneous response (Falkenstein, Hohnsbein, Hoormann, & Blanke, 1991; Gehring, Goss, Coles, Meyer, & Donchin, 1993). In the RDoC performance monitoring subconstruct, ERN modulation is mainly grounded on the Mismatch Theory (Falkenstein et al., 1991). The Mismatch theory states that ERN reflects the mismatch degree between the intended correct response and the erroneous response. ERN works, therefore, as an online error-detection system that is able to monitor and reduce the disruptive answers.

Similarly, N2 is a negative wave component peaking about 200–350 ms after stimulus onset that have been associated with the process of monitoring response conflicts between a predominant but inappropriate response pattern, and an incompatible but more adaptive response (Folstein & van Petten, 2008; Larson et al., 2014). Nevertheless, there is a longstanding debate whether N2 specifically reflects response inhibition or the broad monitoring process (Folstein & van Petten, 2008; Donkers & van Boxtel, 2004). For instance, the go/no-go task demands conflict monitoring along with inhibition. Arguments in favor of the inhibition hypothesis state that N2 amplitude predicts inhibition efficiency and that N2 is still increased on no-go stimuli, even when go and no-go trials occur with an equal frequency. Otherwise, the monitoring hypothesis argue that N2 is not modulated by response priming, requiring inhibition and that the neural source of N2 is co-localized with ERN in the anterior cingulate cortex. From the matrix analysis, RDoC is in accordance with the overlap process of monitoring in ERN/N2. One point of intersection between hypotheses is that the increased amplitude of N2 is associated with the effective recruitment of cognitive resources for the subsequent tasks (Braver, Barch, Gray, Molfese, & Snyder, 2001). That is, N2 amplitude may negatively affect the behavioral performance.

N450 shows a similar structural distribution to N2 and peaks about 450 ms after stimulus onset, with a larger amplitude following incongruent stimuli than congruent stimuli (West & Alain, 1999; West & Bailey, 2012). Despite not so widely studied as ERN and N2, the N450 plays equally a critical role in conflict detection and monitoring, and is often elicited by the Stroop paradigms (Liotti, Woldorff, Perez, & Mayberg, 2000).

Clinical findings

Larson and Clayson (2011) evidenced that larger ERN amplitudes are associated with improved executive control processes in healthy individuals, such as performance monitoring. On the other hand, decreased ERN amplitudes are associated with poorer performance monitoring in psychiatric, neurological and behavioral disorders characterized by high levels of disinhibition (Patrick et al., 2013), as attention deficit hyperactivity disorder (Geburek, Rist, Gediga, Stroux, & Pedersen, 2013), AD (Mathalon et al., 2003) and Parkinson's disease (Seer, Lange, Georgiev, Jahanshahi, & Kopp 2016), juvenile violent offenders (Vilà-Balló, Hdez-Lafuente, Rostan, Cunillera, & Rodriguez-Fornells, 2014), children with concussions (Moore et al., 2015), and psychosis (Chan, Trachik, & Bedwell, 2015). The failure in detect errors may help to explain why impulsive individuals are more likely to replicate disruptive behaviors. Interestingly, reduced error detection seems to be specific of externalizing manifestations of behavior. In internalizing traits, a dissociable effect is expectable, given the hypervigilance and oversensitivity to failure (Olvet & Hajcak, 2008).

In what concerns to N2 amplitude, abnormalities are documented in juvenile violent offenders (Vilà-Balló et al., 2014), traumatic brain injury (Reza, Ikoma, Ito, Ogawa, & Mano, 2007), depression (Clawson, Clayson, & Larson, 2013; Connel, Danzo, & Dawson, 2018), and drinking disorders (Connel et al., 2018).

The amplitude of N450, on the other hand, seems to be more sensitive to aging effects in cognition, with the differences between younger and older adults indicating a poorer performance in conflict detection in older adults (West, 2004; West & Alain, 2000).

RDoC WM construct

Definition

RDoC describes WM as a higher-order cognitive function responsible for the active maintenance, manipulation and flexible updating of goal/task relevant information. These representations in WM are frequently temporary, but may be internally maintained in the absence of external cues. WM underlies attentional control and affects other cognitive operations such as reasoning, language comprehension and learning, highlighting the critical role of WM in everyday functioning (Baddeley, 2007; Barr et al., 2014).

Measurement paradigm

Traditional neuropsychological instruments to assess WM through the collection of behavioral data are retrieved from Wechsler Scales; specifically, the letter-number sequencing and spatial span (Wechsler, 1997a, 1997b). Although there are several variations of span tasks, usually a sequence of stimuli is presented requesting the participant to reproduce the sequence in the same or in the inverse order. Additional orders may be given as a distractor (Guevara et al., 2018; Scharinger, Soutschek, Schubert, & Gerjets, 2017). Experimental paradigms, as the *N*-Back, are widely used to explore the physiological correlates that are elicited when the participant is instructed recognize the stimulus presented "N" trials back (Gevins & Cutillo, 1993).

Electrophysiological correlates

Gamma-band oscillations play an important role in the synchronization of the cortical networks that are involved in short-term cognitive processes, as WM (Babiloni et al., 2004; Schneider, Debener, Oostenveld, & Engel, 2008). Reduced gamma activity underlies poorer performance on WM tasks (Barr et al., 2014).

Regarding theta, the oscillations in this power band range from 4 to 7 Hz and are linked to the integration of information and neuronal communication between different brain areas, playing a significant role on cognitive control, learning and memory (Basar, Schürmann, & Sakowitz, 2001; Kahana, Seelig, & Madsen, 2001; Kirk & Mackay, 2003). Studies have reported the connection between theta activity and WM, with a coherent functioning associated with higher WM performance (Langer, von Bastian, Wirz, Oberauer, & Jänke, 2013).

Despite less explored in the scientific community, delta-band oscillations (0–4 Hz) relate to attention and inhibition cognitive processes and appear to be implicated in the internal processing of mental tasks (Fernández et al., 1995; Harmony, 2013; Harmony et al., 1996).

Clinical findings

Gamma waves are sensitive to aging and to the prolonged exposure to stress (Barr et al., 2014; Marshall, Cooper, Segrave, & Geeraert, 2015) and are further associated with clinical diagnosis of schizophrenia and mild cognitive impairment, with studies reporting changes in the early stages of these conditions (Barr et al., 2010; Missonnier et al., 2012). Importantly, the detection of subtle alterations in brain processing shows potential to enhance the probability of early diagnosis and, subsequently, interventions targeting the affected processes.

Significant differences in theta power were found between healthy adults and patients with diagnose of schizophrenia or fibromyalgia during the performance of a WM task (González-Villar, Pidal-Miranda, Arias, Rodríguez-Salgado, & Carrillo-de-la-Peña, 2017; Schmiedt, Brand, Hildebrandt, & Basar-Eroglu, 2005). In fact, patients with fibromyalgia had exhibited a similar performance to healthy controls during the task, but significant differences were found in theta power, unveiling lower connectivity (González-Villar et al., 2017).

In what concerns to the discriminative capabilities of delta-band regarding WM, a study with mental calculation exercises, which is a task that actively involves the recruitment of WM, has reported increased delta power during task performance (Fernández et al., 1995).

In sum, differences between clinical samples and healthy controls were found in frequency bands associated with WM, even in the absence of significant differences in behavioral data. This highlights the need to consider the results from the proposed RDoC physiological outcomes when interpreting the results from the neuropsychological assessment and when designing rehabilitation and stimulation programs.

Conclusion

Historically, neurophysiology and neuropsychology progressed somewhat as separate areas of knowledge (Connolly & D'Arcy, 2000; Walhovd & Fjell, 2003). Clinicians used physiological index to assess sensory functions and neuropsychological tests to measure cognitive functions (Connolly & D'Arcy, 2000). Consequently, it was not clear the role of basic electrophysiological processes in neuropsychological assessment to unveil the neural underpinning of cognitive functioning.

In recent years, however, significant advances in the interplay between the two areas of knowledge have been observed. Now, and from the reviewed evidence, it is possible to connect correlates of cognitive processing at both psychological and physiological levels grounded on solid theories and robust empirical data while recognizing its clinical value.

The most recent research framework conceptualized to improve the understanding of mental conditions – the RDoC – reflects these endeavors. Interestingly, and almost in a paradoxical way, this review highlights that modern neuropsychological assessment methods proposed by RDoC are not really modern. In line with the focus of this special issue, it is evidenced that the paradigms proposed by RDoC are not innovative and are based on classical neuropsychological paradigms. For the RDoC initiative, the gold standard practices of neuropsychological assessment are crucial since these tasks

Table 1. RDoC matrix – cognitive systems domain.

Constructs	Subconstructs	Paradigms	Physiology
Attention		Dual-task paradigm	ERP: P3 fMRI: sensory areas from peripheral to central
Perception	Visual perception	Face and emotion identification	fMRI: BOLD activation of cortical regions ERP components Oscillations
	Auditory perception	Oddball detection	fMRI ERP: P3
Declarative memory		Delayed recall	fMRI: frontal/temporal coordinated oscillations
Language		Naming; detection and classification of semantic relationships	N400, P600/late positivities
Cognitive control	Goal selection updating, representation, maintenance	Task switching	Gamma
	Inhibition/Suppression	go/no-go, stop-signal reaction time	Alpha
	Performance monitoring	Flanker, Stroop	ERN, N2, N450
WM	Active maintenance flexible updating limited capacity interference control	Complex and simple span tasks, n-back	Delta, gamma, theta

Note: adapted from https://www.nimh.nih.gov/research-priorities/rdoc/constructs/rdoc-matrix.shtml.

have an extensive empirical use and their measures provides robust neural correlates. This is consistent with the empirically based ambitions of RDoC. These paradigms were targeted considering the development of computerized versions that allow to collect neurobiological measures with minimal deviations from the original versions of neuropsychological tests. So, the advances in neuropsychology anchored in RDoC are not observable in terms of innovative paradigms, but rather in terms of the outcomes that may be obtained from these classical neuropsychological tasks.

The behavior unit of analysis may be integrated with physiological outcomes while mapping distinct cognitive constructs simultaneously. The dimensional properties of RDoC constructs allow to implement assessment batteries that may be developed to answer to individual-specific clinical concerns. From this perspective, the advances in neuroscientific knowledge may inform current methods of neuropsychological assessment. In the current work, these advances were reviewed in the RDoC Cognitive Systems domain to provide guidance to clinical neuropsychologists when incorporating behavior and physiological units of analysis in neuropsychological assessment. Table 1 systematizes the main findings. Importantly, physiology is a unit of analysis that offers non-invasive efficient possibilities, as EEG, which is a relatively inexpensive method for the study of brain–behavior relations (Light et al., 2010; Pasion et al., 2016b).

A comprehensive and specific identification of neuropsychological deficits may be further used as targets to customize neurorehabilitation programs. Barwood et al. (2011) demonstrated that after 2 months of low-frequency repetitive transcranial magnetic stimulation, an improved (more negative) N400 was found in the active stimulation group, compared to the placebo group. Despite similar amplitude measures in both chronic non-fluent aphasia groups at the baseline, N400 modulation was improved subsequent to low-frequency repetitive transcranial magnetic stimulation. The assessment of neural oscillations is also proposed as a practical and objective indicator to monitor the progress of the undergoing intervention (Yeung et al., 2016). Moreover, neurophysiological correlates provide information on clinical recovery. Progressive recovery of distinct ERPs is correlated with neuropsychological results (Reinvang, 1999). For example, P3 amplitude predicts clinical recovery after traumatic head injury (Reinvang, 1999) and the changes documented by Barwood et al. (2011) remained stable in the following 12 months (Barwood et al., 2012).

Once more, effective neurorehabilitation programs become available, early and accurate diagnosis will be even more crucial. The study on biomarker in time and frequency domains is advancing our knowledge on risk factors, allowing to prevent the onset of clinical conditions (Yeung et al., 2016). Some studies further documented that subtle changes in the frequency domain may be detected in the early stages of the disease (Barr et al., 2010; Missonnier et al., 2012), indicating that band analysis is a valuable tool subserving early and accurate diagnosis. Of high importance, it is very common not to find significant differences in behavioral parameters while these differences may be detected at the neurobiological level (e.g. González-Villar et al., 2017; Langer et al., 2013; Pasion et al., 2016a).

The physiological tools show interesting possibilities to neuropsychological assessment and treatment of vulnerable and non-communicative patient populations. Neuropsychological assessment based on conventional tests is dependent on the ability to comprehend the instructions, to communicate and respond appropriately (Connolly & D'Arcy, 2000). Some neurological conditions, as traumatic brain injury, may affect significantly comprehension, motor and language functions in the first weeks, limiting the validity of neuropsychological-behavioral assessment (Marchand et al., 2002). In turn, physiological paradigms use simple stimuli, increasing the clinical utility when studying the underlying processes of the brain. Furthermore, ERPs and brain oscillations may be recorded in the absence of a behavior response. Record subtle cognitive activity using EEG techniques from widely accepted assessment methods offers, subsequently, a major advantage in the assessment of non-communicative and vulnerable patient populations.

ERPs are also relatively independent from extraneous variables that may affect behavioral measures (Parra et al., 2012; Walhovd & Fjell, 2003). For example, the oddball paradigm appears to be insensitive to transcultural variations, a variable that is a challenging issue in neuropsychological testing settings (Parra et al., 2012). However, the fatigue effects should be prevented since many trials must be included in tasks to produce a robust signal-to-noise ratio. Nevertheless, some studies reported the sensitivity of neurophysiological correlates to control external factors, such as fatigue (Bonnefond et al., 2008). The alpha band is sensitive to fatigue and engagement effects, demonstrating correlations with subjective evaluations (Bonnefond et al., 2008). This may improve the ecological validity of neuropsychological assessment by considering external factors that might influence the person's performance on behavioral measures.

In conclusion, neurophysiological outcomes are important to consider in neuropsychological assessment, providing relevant information that can complement and support behavioral data acquired in this area. Although the RDoC matrix is research-oriented, and sound bridges with clinical practices are still to be developed, the integration of multiple levels of analysis under its aegis allows to obtain a more detailed and complete neuropsychological characterization with high potential to be translated into better intervention strategies.

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