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Criticalities of Executive Functions (EFs) research in Gambling Disorder: between the behavioural and neurophysiological markers

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ABSTRACT

The need to use different and heterogeneous approaches and methodologies to investigate the phenomenon of pathological Gambling Disorder (GD) arises from a substantial difference in the literature results emerging in this area. Furthermore, investigating the executive functioning (EFs) of subjects with GD provides important information that can influence the treatment setting of these populations. In the present paper the involvement of EFs in the present disorder was investigated. The cognitive functioning of subjects with GD was deepened, both through the study of the cerebral correlates of executive functioning in GD and through empirical studies that investigate the behavioural deficits of GD. Furthermore, we considered the role of some specific behavioral tasks (such as the Iowa Gambling Task, IGT) for the assessment of EFs. Finally, the relationship between EFs and some other crucial factors, such as reward sensitivity, were focused. Indeed, the behavioural aspects of GD are multiple, and they include not only traditional functions such as inhibitory control and reduced levels of self-control, but also high sensitivity to reward.

Keywords: gambling disorder; behavioural addictions; EFs; reward sensitivity; IGT

1. Introduction: what role do Executive Functions play in Gambling Disorder?

Gambling Disorder (GD) is now recognized as a clinical disorder in the International Classification of Disease (ICD-11; World Health Organization, 2019) and the Diagnostic and Statistical Manual of Mental Disorders (DSM-V; American Psychiatric Association, 2013). It has been defined as *"a pattern of persistent or recurrent gambling behaviour, which may be online (i.e., over the internet) or offline, manifested by:*

1. impaired control over gambling (e.g., onset, frequency, intensity, duration, termination, context);

2. increasing priority given to gambling to the extent that gambling takes precedence over other life interests and daily activities;

3. continuation or escalation of gambling despite the occurrence of negative consequences" (ICD-11).

Prevalence of Gambling Disorder varies by socio-cultural background (about 0.2/0.3% in the general population, according to the DSM-V), is higher among males and has a typical onset in adolescence or young adulthood, in association with higher levels of impulsivity.

Individuals with GD are not a homogeneous group but are characterized by different nuances for example in their preferred form of play, motivation for gambling, and probably also in terms of executive functioning, as suggested by Mallorquí-Bagué and colleagues (2018).

This contribution discusses the role that Executive Functions (EFs) play in GD. Impairments of EFs typically underlie addictive behaviours (Hester and Garavan, 2004), hence it is essential to investigate EFs dysfunction also in GD. This is especially relevant since EFs deficits may affect an individual's capacity to take advantage of psychosocial therapies for GD (e.g., higher levels of impulsivity in decision-making significantly impact treatment drop-outs) (Leblond et al., 2003).

EFs can be conceived as a set of cognitive functions that are at the heart of higher cognition. Baddeley and Hitch (1974) coined the term "central executive" for EFs and Lezak defined it as "a component of individual behavior that concerns how behavior is exhibited" (Lezak, 1982). Actually, the "EFs" term expands the three-component models of Miyake and colleagues (2000) and Diamond (2013) and encompasses a broad range of functions, including inhibitory control, working memory, cognitive flexibility, decision-making, conflict monitoring, and the putative link of these functions to decisional mechanisms linked to reward (Moccia et al., 2017) and multiple alternative descriptions of EFs that correspond to the various theories of cognition and neuropsychology have been formulated.

EF incorporates higher-level cognitive processes such as to plan and implement a behavior, to predict the (more or less advantageous) outcomes of an action, and the capacity to regulate the behavior depending on contextual input (Lezak et al., 2004). The cognitive processes necessary for the effective execution of any sophisticated behavioural or cognitive task are planning, judgment, decision-making, set-shifting, anticipation, and reasoning. In the field of addiction, the ability to suppress unnecessary input stimuli and output responses, as well as the prevention of improper reactions, have also been highlighted as essential (Balconi et al., 2015b, 2015a, 2018).

To better understand the role of a deficit of EFs in GD, the present paper focused on both the behavioural and neurophysiological markers of these dysfunctions. The first section discusses the behavioral markers of EFs deficit in GD, with a specific focus on the decision-making process. In the second section, the neurophysiological evidence of EFs deficits in GD has been described. Finally, some of the main criticalities of research on EF in the context of gambling were reported.

2. Behavioral markers of EFs deficit in GD: a specific focus on the decision-making process

Several studies have found a general trend in the behavioral impairment of EFs in GD. Indeed, when GD participants were compared to non-GD participants in multiple neuropsychological tests, they showed impairments in planning, cognitive flexibility, and behavioral inhibition (Ledgerwood et al., 2012). By employing a complete neuropsychological battery testing EFs, another study found that GD and alcohol-dependent individuals had lower EFs efficiency in terms of inhibitory control, timing, mental adaptability, and planning (Goudriaan, Oosterlaan, de Beurs, et al., 2006). In a different work (Zhou et al., 2016), GD patients reported an impairment in verbal fluency, working and episodic memory. Lastly, the conduct of patients with GD is hindered at the Iowa Gambling Task (IGT), a classical task developed to assess decision skills in ambiguous and risky conditions (Brevers et al., 2012). In this context, research has also found that GD patients exhibit cognitive abnormalities in a variety of areas, including reduced inhibitory control performance as well as augmented motor impulsivity (Van Holst et al., 2012).

However, it has not yet been determined in previous neurocognitive works if these deficits arose from the pathophysiology of recurrent gambling or reflected abnormalities that may occur prior to symptoms and exist in vulnerable individuals.

A lack of control of the impulsive behavior and the consequent negative outcomes consists of another important feature that might be linked to EF deficits in

GD. In multiple previous works, markers of impulsivity derived from tasks and questionnaires have been associated with GD (Ioannidis et al., 2019). The loss of control over impulsive behavior has been linked before to abnormalities in the functioning of the frontal brain regions associated with EFs (Hinson et al., 2003). In fact, impulsivity and attention deficiency have been linked to GD: on attention tests, GD patients performed worse than control participants, and they displayed more childhood behaviors associated with attention impairment. In recent times, neurocognitive markers of impulsive behavior, like the performance at the Go/No-Go task and the Barratt Impulsiveness Scale results, have shown that patients with GD have greater levels of impulsivity than controls, giving emphasis to the construct of impulsivity when GD is presented (Angioletti et al., 2020; Fuentes et al., 2006). Also, meta-analyses indicate significant deficits in individuals with GD in cognitive flexibility, attentional set-shifting, attentional bias, and a compulsivity-related performance deficit (Van Timmerman et al., 2018).

In addition, the IGT has been thoroughly studied and adopted for measuring the impairments in decision processes of a number of clinical groups, ranging from those with frontal lobe dysfunction to those with substance use disorder (SUD) to those with GD. Interestingly, previous research has shown that the manifest behavior of individuals with GD on the IGT is equivalent to that of SUD patients (Goudriaan et al., 2006).

With two separate versions of the IGT, a more recent study attempted to define decision-making deficiencies in patients with GD and analyze distinguishing aspects in two types of decision-making: under uncertainty and under risk (Ochoa et al., 2013). According to the results, the majority of individuals with GD showed decision processes impairments, and these deficits have been commonly ascribed to a "myopia for the future" rather than a dislike of being punished. Moreover, patients with GD exhibited anomalous decision behavior more in regard to risky decisions at the IGT (related to task knowledge, EFs, mechanisms of cognitive control and impulsivity) than in relation to decisions made under ambiguity. It is worth mentioning that distinct patterns of impaired behavior are engaged when individuals with GD face a decision dynamic, and predictions change on the basis of the reinforcements (Ochoa et al. 2013).

Furthermore, a study by Brand and colleagues (2007) sought to investigate the temporal dynamics of play at the IGT and revealed that the individual makes decisions under uncertainty more in the early stages of the task (the first trials), in which the understanding of the rules is still not clear and the game is mainly based on the elaboration of emotional feedback, while the decision-making process under risk would seem to mark the last phases of the task, when the game dynamics become less ambiguous and the task requires high-order cognitive functions, including EFs, like cognitive flexibility, ranking and monitoring. As a result, while Bechara (2001) claimed that participants should attend their somatic states and insights in order to

perform well on this task (in line with the Somatic Marker Hypothesis, Bechara et al., 1999), it seems possible to argue that, in line with other works (Brand et al., 2007), emotions and somatic states count for decisions, but EFs are also needed to complete a functional decision-making process.

Taken together, these observations indicate that GD patients with lower inhibitory control, increased impulsivity, and poor decision-making capacity require particular treatment interventions based on learning strategies to cope with cravings, and developing new, healthy patterns of behavior to replace addictive behavior or financial literacy techniques (Goudriaan et al., 2008). It has also been recommended that therapies for effectively treating patients with GD include ways for recognizing impulsive reactions prior to action, for encouraging people to reflect and consider the future implications of a choice, to control the behavior, as well as finding suitable different options (Álvarez-Moya et al., 2011).

3. Neurophysiological evidence of EFs deficits in GD

Behavioral deficits observed in individuals with GD have also been associated with deficits at the neurophysiological level, not only for decision-making (to which a specific focus was dedicated in the previous section) but also for a wider range of EF.

In addiction studies, researchers have often focused on the neurocognitive processes and functions supported by the prefrontal cortex (PFC) (Goldstein & Volkow, 2011).

Despite the PFC's deeply interconnected function, two separate PFC systems have been linked to various subcomponents of the frontal functioning. The "cool" EFs network encompassing the anterior cingulate cortex (ACC), lateral inferior cortex (LIC), and dorsolateral prefrontal cortex (DLPFC) supports working memory, inhibitory control, task switching, and conflict monitoring (Badre and D'Esposito, 2009; Koechlin et al., 2003), whereas the "hot" EFs network comprehends the ventral, medial, and orbitofrontal structures (VMPFC, OFC) and supports the valuation, emotion regulation, and decision-making (functions involved in reward/emotion-related aspects) (Balconi et al., 2015; Bechara and Linden, 2005; Peters and Büchel, 2010).

EFs engage a number of regions within the PFC (Coull et al., 2004), cingulate and parietal cortex (Van Den Heuvel et al., 2003), as well as subcortical structures highly connected to the PFC, such as the thalamus, putamen and caudate nucleus (Monchi et al., 2001). It is therefore likely that EF impairments, such as those identified in individuals with GD, are linked to malfunctions and aberrant patterns of these areas and networks (Moccia et al., 2017).

Behavioural findings appear to be supported by brain imaging data, which show

abnormal cerebral blood flow variations in the PFC of individuals with GD (Grant et al. 2016), specifically in the VMPFC and cortico-basal ganglionic-thalamic pathways (Potenza et al., 2003b, 2003a), lateral prefrontal cortices (considered the neurological basis of executive functioning (van Holst et al., 2012; Wager and Smith, 2003; Zakzanis et al., 2005), right middle frontal gyrus (van Holst, van der Meer, et al., 2012), and an augmented responsivity of the left part of the dorsal ACC (Quaglieri et al., 2020).

GD is characterized by white matter abnormalities and reduction in cortical thickness (Yip et al., 2013; Joutsa et al., 2011). GD studies have shown resting state-MRI hyperconnectivity in regions within putamen, amygdala, and medial frontal gyrus and hypoconnectivity in caudate, cingulate and thalamus (Tolomeo et al., 2022).

Also, the reward circuit contributes to GD. It includes both subcortical and cortical regions (PFC included) and, via the dopaminergic pathways, it may promote food consumption, social reproduction, as well as neural reactions to "unnatural rewards" (such as monetary incentives), which can lead to obsessive behaviors such as gambling (an equivalent process take place for drugs) (Comings and Blum, 2000). Within this process, the striatum has been implicated in the expectation of monetary rewards (Miedl et al., 2012; Power et al., 2012): indeed, bilateral dorsal striatum increased activity was found in GD patients, which was linked to strong action-outcome association (Van Holst et al., 2012), this, in turn, might find an explanation in an overestimation of the gambling results. The hyperactivation of the dorsal striatum would therefore appear connected with a greater level of the pursuit of rewards, that might represent a compensation strategy for the lack of rewards in individuals with GD (Van Holst et al., 2012); on the other hand, the reward processing seems supported by the ventral section of the striatum (Miedl et al., 2012).

In terms of PFC integration, the fronto-striatal cortical circuit, which includes reward processing, regulation, and the preparation of a motor behavior, is critical for EF (Robbins, 2007). Hyperactivation of the striatum caused by more severe GD clinical symptoms resulted in a poorer capacity to regulate gambling behavior. Individuals with GD display deficiencies in self-regulation and a greater degree of reward-seeking behavior, which may be associated with fronto-striatal dysfunction. The dopaminergic system and the brain pathways linking subcortical structures, such as the basal ganglia and limbic areas, and cortical anterior areas are consequently unbalanced, resulting in a lack of control over gambling behaviour (Moccia et al., 2017).

4. Criticalities of EFs research in the context of gambling

Notwithstanding the importance of this family of functions in the manifestation of GD, there is currently a lack of study in this area, and the results are inconsistent. For instance, the majority of research did not look at whether EF deficits are independent of abnormalities in fundamental cognitive functions.

Without claiming to be exhaustive, below some critical points that need to be developed in the following research works are reported.

Firstly, despite several meta-analyses and systematic reviews have addressed EFs in GD (e.g., Ioannidis et al., 2019; Quaglieri et al., 2020; van Timmeren et al., 2018), there is no indication that GD patients have a broad and generalized EF deficit. For instance, Mallorquí-Bagué and colleagues (2018) suggested executive functioning may differ based on subtypes of individuals with GD. Also, while EF impairments are mentioned in the ICD-11 definition of the GD, there is no devoted in-depth section on the EF deficits in the description of the disorder in diagnostic manuals. Such integrations could be important to advance the research field.

Second, a large number of research studies suffer from methodological flaws. The major explanation for these discrepancies is because several works only looked at a singular EF, many findings are limited to not numerous samples, either they frequently neglected to account for concomitant diseases (such as comorbid alcohol use disorder, depression, substance use disorders, nicotine dependence, anxiety disorders, and antisocial personality disorder; Lorains et al., 2011) and medicine usage.

Furthermore, since much of this study did not involve clinical representative samples, but mainly samples with GD and other comorbid conditions, the specificity of EF impairments in GD has yet to be clearly determined. Due to the inclusion of only treatment-seeking individuals, sampling bias may result in convenience groupings (Lorains et al., 2011). Also, most patients with GD seem to look for treatment not for GD but rather for diseases in comorbidity (Winters and Kushner, 2003). Further, statistically inferential tests cannot be applied to reduced clusters of participants, therefore a descriptive approach only could restrict findings generalization.

Lastly, much significant research has been conducted without a full neurocognitive evaluation, resulting ultimately based upon partial evidence.

As a result of the aforementioned constraints, more research using complete neuropsychological and neurophysiological assessment on larger, typical, impartial, ecologically valuable clinical populations displaying GD is indispensable.

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