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Review article

Compulsivity-related neurocognitive performance deficits in gambling disorder: A systematic review and meta-analysis

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ABSTRACT

Compulsivity is a core feature of addictive disorders, including gambling disorder. However, it is unclear to what extent this compulsive behavior in gambling disorder is associated with abnormal compulsivity-related neurocognitive functioning. Here, we summarize and synthesize the evidence for compulsive behavior, as assessed by compulsivity-related neurocognitive tasks, in individuals with gambling disorder compared to healthy controls (HCs). A total of 29 studies, comprising 41 task-results, were included in the systematic review; 32 datasets (n = 1072 individuals with gambling disorder; n = 1312 HCs) were also included in the meta-analyses, conducted for each cognitive task separately. Our meta-analyses indicate significant deficits in individuals with gambling disorder in cognitive flexibility, attentional set-shifting, and attentional bias. Overall, these findings support the idea that compulsivity-related performance deficits characterize gambling disorder. This association may provide a possible link between impairments in executive functions related to compulsive action. We discuss the practical relevance of these results, their implications for our understanding of gambling disorder and how they relate to neurobiological factors and other 'disorders of compulsivity'.

1. Introduction

1.1. Rationale

Pathological gambling has recently been reclassified as a behavioral addiction and renamed as Gambling Disorder (DSM-5; American Psychiatric Association, 2013). This decision was largely based on clinical and neurobiological similarities with substance-use disorders (Fauth-Bühler et al., 2017; Romanczuk-Seiferth et al., 2014). Similar to drug addiction, symptoms of gambling disorder include repeated unsuccessful efforts to stop gambling, feeling restless or irritable when attempting to stop and diminished ability to stop gambling despite the negative consequences of gambling. Gambling disorder was previously classified as an impulse control disorder and has long been associated with higher impulsivity (Verdejo-García et al., 2008). Now that gambling is reclassified as a behavioral addiction, there is an increased need to focus on the compulsive aspects of the behavior, which may be central to understanding the pathology of gambling disorder (e.g. El-Guebaly et al., 2012; Leeman and Potenza, 2012), and addiction in general.

Addiction can be viewed as the endpoint in a series of transitions: from initial goal-directed through habitual to eventually compulsive addictive behavior (Everitt and Robbins, 2005). Phenomenological models of addiction also highlight the motivational shift from impulsivity to compulsivity (El-Guebaly et al., 2012). Self-report questionnaires assessing addiction-specific compulsive tendencies indeed indicate the presence of compulsive behavior in addictive populations (Anton et al., 1995; Blaszczynski, 1999; Bottesi et al., 2014; Vollstädt-Klein et al., 2015). Moreover, in addition to compulsive drug use behavior, impairments in general compulsivity-related executive functions, such as perseverative behaviors or cognitive inflexibility, might also be related to addiction (Fineberg et al., 2014). Because gambling disorder may provide a model of drug-free addiction, it offers the opportunity to investigate compulsivity as an endophenotype for addiction. Other behaviors, such as food, sex, and Internet addiction, can potentially be compulsive too (Morris and Voon, 2016). However, these behaviors were outside the scope of the current review, as they are not included under the 'Substance-related and Addictive Disorders' category in the DSM-5 due to insufficient research.

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Studies investigating compulsivity, i.e. the performance of repetitive acts despite the negative consequences, in individuals with gambling disorder are scarce. This may be due to the complex, multi-faceted nature of the construct. Indeed, compulsivity can be conceptualized in various ways, which seem to differ between disorders and descriptions (Yücel and Fontenelle, 2012). Importantly, and as opposed to impulsivity, the number of research instruments to assess compulsivity is limited. Therefore it has been suggested that, although useful as a concept for clinicians, compulsivity "is too ambiguous and confusing for research studies of the topic" (Yücel and Fontenelle, 2012). On the other hand, new definitions of compulsivity have been proposed which account for its multi-dimensionality and offer opportunities to systematically study the mechanisms that contribute to compulsive behavior (e.g. Fineberg et al., 2010; Dalley et al., 2011).

Compulsive behavior is likely to result from disruptions in various cognitive processes, including attention, perception, and the regulation of motor or cognitive responses. A recent theoretical review of compulsivity by experts in this field has proposed a framework in which compulsivity is subdivided into four separate, neurocognitive domains: contingency-related cognitive flexibility, task/attentional set-shifting, attentional bias/disengagement, and habit learning (Fineberg et al., 2014). Each of these domains entails a separate component of compulsivity with a separate neural circuitry (Fineberg et al., 2014) and can be operationalized with specific neurocognitive tasks (see Table 1). One critical component of compulsive behavior, mainly associated with repetitive behavior, is the inability to adapt to a situation flexibly. Neurocognitive tasks assessing cognitive (in)flexibility either (i) manipulate contingencies, which is mainly dependent on learning/unlearning behavior (contingency-related cognitive flexibility), (ii) manipulate attentional response modes (task/attentional set-shifting) or (iii) test the ability to inhibit a prepotent, automatic response (attentional bias/disengagement) (Fineberg et al., 2014). Another component that may give rise to compulsivity is (iv) over-reliance on habit learning: the tendency of actions that are often repeated to become automatic and insensitive to goals. For heuristic purposes, we chose to use these four domains as a framework to organize and investigate the evidence for compulsivity in gambling disorder.

1.2. Objectives

The central aim of this systematic review and meta-analysis is to summarize and integrate, for the first time, the empirical evidence for impairments in compulsivity-related neuropsychological functions in gambling disorder. Accordingly, we set out to answer the following question (following PICO-criteria): in individuals suffering from gambling disorder, is there evidence for compulsive behavior, compared to HCs, as assessed by neurocognitive measures? To this end, we systematically reviewed the literature on gambling disorder to include all experimental studies measuring one of the four components of compulsivity (Table 1). In addition, meta-analyses were performed for all separate tasks within each domain (with a minimum of 3 studies per task) to summarize the available knowledge. We hypothesized that compulsivity-related neuropsychological functions are impaired in individuals with gambling disorder compared to HCs.

2. Methods

This systematic review and meta-analysis was conducted and reported in accordance with the Preferred Reporting Items for Systematic reviews and Meta-Analyses for Protocols 2015 (PRISMA-P 2015) guidelines (Moher et al., 2015) and has been registered in PROSPERO International Prospective Register of Systematic Reviews (crd.york.ac.uk/prospero, registration number: CRD42016050530). The PRISMA for Protocols (PRISMA-P) checklist for the review is also included in Supplementary File 1.

2.1. Information sources and search strategy

We started by searching the WHO International Clinical Trials Registry Platform (WHO ICTRP) and ClinicalTrials.gov for potentially eligible ongoing trials. Original articles were searched using Ovid MEDLINE, Embase and PsycINFO. The searches were conducted in August 2016 and updated in February 2017.

A scoping search identified the following key concept [] combinations: [gambling disorder] AND ([compulsion] OR [neuropsychological tests] OR [measured relevant test parameters]). Subsequently, these key concepts were adapted for each bibliographic database applying appropriate (controlled) terms, database specific search fields and syntaxes. See Appendix A (Supplementary data) for a fully detailed search strategy.

It should be noted that tasks assessing disorder-specific attentional bias were not considered, because behavioral differences between individuals with gambling disorder and HCs are not (necessarily) related to cognitive flexibility per se, but rather to the addiction itself and, therefore, not relevant for the cross-diagnostic endophenotype of compulsivity. Moreover, disorder-specific attentional bias might reflect multiple underlying processes (Field and Cox, 2008). For these reasons,

Table 1
Four domains of compulsivity.

Neurocognitive domain[a]	Definition	Task	Outcome (# studies reporting this outcome)	# studies in GD
Contingency-related cognitive flexibility	Impaired adaptation of behavior after negative feedback	Probabilistic Reversal Learning Task	Number of reversals (1); money won (1); perseverative errors (1); reversal cost (1)	4
		Card Playing Task	Number of cards played (1); perseveration level (categories) (2)	3
		Deterministic Reversal Learning Task	Mean error rate (1)	1
		Contingency Learning Task	Commission/Perseveration errors (1)	1
Task/attentional set-shifting	Impaired switching of attention between stimuli	Wisconsin Card Sorting Task	Perseverative errors (8); total trials (1)	9
		Intra-Extra Dimensional Set Shift	Total errors (4)	4
		Switch task	Accuracy (1)	1
Attentional bias/disengagement	Impaired shifting of mental sets away from stimuli	Stroop task	Interference index (8); RT/% incorrect (4)	12
		Trail Making Task (B)	Time to complete (4)	4
Habit learning	Lack of sensitivity to goals or outcomes of actions	Two-step decision task	Model-based and model-free choices	0
		Fabulous Fruit Game	Slips-of-action errors	0
		Devaluation task	Valued versus devalued choice ratio	0

GD = Gambling Disorder; RT = Reaction Time.
[a] Domains from Fineberg et al. (2014).