



## Review

# Cross-species approaches to pathological gambling: A review targeting sex differences, adolescent vulnerability and ecological validity of research tools<sup>☆</sup>

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## ABSTRACT

Decision-making plays a pivotal role in daily life as impairments in processes underlying decision-making often lead to an inability to make profitable long-term decisions. As a case in point, pathological gamblers continue gambling despite the fact that this disrupts their personal, professional or financial life. The prevalence of pathological gambling will likely increase in the coming years due to expanding possibilities of on-line gambling through the Internet and increasing liberal attitudes towards gambling. It therefore represents a growing concern for society. Both human and animal studies rapidly advance our knowledge on brain-behaviour processes relevant for understanding normal and pathological gambling behaviour. Here, we review in humans and animals three features of pathological gambling which hitherto have received relatively little attention: (1) sex differences in (the development of) pathological gambling, (2) adolescence as a (putative) sensitive period for (developing) pathological gambling and (3) avenues for improving ecological validity of research tools. Based on these issues we also discuss how research in humans and animals may be brought in line to maximize translational research opportunities.

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## Contents

1. Introduction.....	2455
2. Pathological gambling in humans.....	2456
2.1. A behavioural addiction.....	2456

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2.2.	Sex differences .....	2457
2.2.1.	General findings .....	2457
2.2.2.	Decision-making .....	2458
2.2.3.	Genetics underlying sex differences .....	2459
2.3.	Adolescent vulnerability .....	2459
2.3.1.	General findings .....	2459
2.3.2.	Cortical–subcortical balance .....	2460
2.3.3.	Monoamine systems .....	2460
2.4.	Ecological validity of research tools related to studies on pathological gambling .....	2461
3.	Animal models of pathological gambling .....	2461
3.1.	Decision-making in animals and neural underpinnings .....	2461
3.2.	Sex differences .....	2463
3.3.	Adolescent vulnerability .....	2463
3.3.1.	General findings .....	2463
3.3.2.	Monoamine systems .....	2464
3.4.	Ecological validity of animal models .....	2464
4.	Optimizing the crosstalk between human and animal research .....	2465
	Conflict of interest .....	2466
	Acknowledgements .....	2466
	References .....	2466

## 1. Introduction

Decision-making plays a pivotal role in daily life as impairments in processes underlying decision-making often result in an inability to make profitable long-term decisions that incorporate expectations of future outcomes (Bechara et al., 1994). In case of pathological gambling such impairments appear to be present as subjects continue to gamble despite the fact that this activity disrupts their personal, professional or financial life (DSM-IV, American Psychiatric Association, 1994; Potenza, 2001). Indeed, pathological gambling is associated with poor decision-making in the Iowa Gambling Task (e.g. Brand et al., 2005; Brevers et al., 2012; Caviedini et al., 2002; Forbush et al., 2008; Goudriaan et al., 2005), a validated task of decision-making encompassing rewards, punishments and uncertainty of outcomes in a complex situation (Bechara et al., 1994). Furthermore, performance in the Iowa Gambling Task is correlated with the severity of problem gambling (Brevers et al., 2012).

The rapid worldwide growth of legalised gambling opportunities has raised concerns over the impact of gambling on public health (Carragher and McWilliams, 2011; Shaffer and Korn, 2002). Epidemiological data suggest that 27% of adults have gambled more than 100 times in their lifetime, and that 10% have gambled more than 1000 times (Kessler et al., 2008). Estimates of lifetime gambling exceed 70% in North America and Western Europe. Although gambling remains a recreational activity for most people, it may become a salient problem for some. The lifetime prevalence of pathological gambling has been found to be between 1.4 and 2% for the United States and Canada (Cox et al., 2005; Welte et al., 2002) and comparable or somewhat lower rates are reported in Western European countries (Volberg et al., 2001). The prevalence of pathological gambling will likely increase in years to come due to the increasing possibility of on-line gambling through the Internet and, in general, more liberal views on gambling itself as well as on increasing gambling opportunities (Donati et al., 2013; McCormack et al., 2012; Wilber and Potenza, 2006). It therefore represents a growing concern for society.

Both genetic (e.g. a polymorphism in the serotonin transporter gene; Ibáñez et al., 2003a) and environmental (e.g. social environment and gambling stimuli; Donati et al., 2013; Potenza, 2013) risk-factors for pathological gambling have been identified, whereas (neuro)psychological studies have unravelled which traits are associated with pathological gambling (e.g. impulsivity), and how the process of decision-making is affected in pathological

gambling (e.g. a shifted risk preference; Brand et al., 2005; Caviedini et al., 2002; Chase and Clark, 2010; Forbush et al., 2008; Goudriaan et al., 2005; van Holst et al., 2012a,b; Ligneul et al., 2013; Potenza, 2013). Furthermore, animal studies are rapidly advancing our knowledge concerning neuro-behavioural and psycho-biological processes underlying decision-making processes related to normal and pathological gambling behaviour (Koot et al., 2012; de Visser et al., 2011; Winstanley et al., 2011). Such studies are crucial as they allow the dissection of processes and factors associated with normal and pathological gambling in a controlled way in experimental settings. Comprehensive reviews on many aspects of pathological gambling already exist (Goudriaan et al., 2004; van Holst et al., 2010; Nussbaum et al., 2011). Here, we will focus on three topics, which have received less attention thus far.

First, as already pointed out by others (Andreano and Cahill, 2009; Cahill, 2006; Viveros et al., 2012) it is becoming increasingly clear that differences in brain-behaviour relationships between sexes matter in many domains of (normal and pathological) behaviour, beyond the reproductive domain. For instance, recent studies have indicated clear sex differences in decision-making (reviews: van den Bos et al., 2013; Overman, 2004; Overman et al., 2004). Here, we therefore review evidence pertaining to sex differences in (the development of) pathological gambling. Second, the particular propensity towards internet-directed behaviour of young children and adolescents may put them at a high risk for progressively developing problematic gambling behaviour, given the increase of on-line gambling opportunities through the Internet. Indeed, studies have suggested that more problematic gambling behaviour may be present in adolescents than adults (Derevensky and Gupta, 2004; Wilber and Potenza, 2006). We therefore also review whether and why adolescence is a (putative) sensitive period for (developing) pathological gambling. We focus on the development of brain circuits underlying decision-making and pathological gambling. Third, currently little is known how in real-life normal or leisure gambling behaviour transforms into pathological gambling behaviour and what triggers or increases gambling episodes in both normal and pathological gamblers. This research barrier is mostly due to a lack of methodological tools to monitor real-life events. Similarly, like in human studies, animal studies may only partly address the processes associated with the context in which decisions are made, such as the social environment. We therefore (briefly) discuss new avenues for bridging the gap between knowledge acquired in the laboratory and monitoring real-life events in normal and pathological gamblers, i.e. to develop

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