A Neuropsychiatric Perspective on Gambling and Morality

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Abstract: Public conceptions of the relationship between morality a

Introduction

Evidence of gambling can be found across cultures and throughout time. Hebraic, Egyptian, Greek and Roman civilizations engaged in various forms of gambling (Quinn, 1892), and the Mahabharat, a central book of Hinduism, describes a gambler who wagers and loses his kingdom and his wife (Mahabharat, 1884). The persistence of gambling for millennia suggests that the behavior may be particularly rewarding at an individual level or important in socio-cultura been described as immoral for millenia. Greek philosophers like Aristotle are reported to have grouped gamblers with thieves and robbers and denounced gambling as wrong and immoral (Quinn, 1892). This sentiment was voiced in other cultures throughout time. In an article on the history of gambling published in England in 1756, gamblers are described as “cheats” and “felons”, and the author states that society would be better off without this group of “harpies”

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compulsivity seems more complex than initially conceptualized (Grant and Potenza, 2006; Potenza, 2007a). In impulse control disorders and drug dependence, it is

intermittent losses resulting in long-term losses and the other two are associated with small immediate rewards and small intermittent losses resulting in long-term gains. As compared to healthy control subjects, those with strokes in the vent control subjects on the Iowa Gambling Task (Petry, 2001b; Cavedini et al., 2002; Bechara, 2003), and amongst subjects with addictions, poor performance was associated with real-life measures of poor functi

(McClure et al., 2004). Prior studies have identif0 0 0 100 0 0 Tm /Fl5;a prefrontal cor

Compared to other psychiatric disorders, relatively few bra

Brain Imaging in Pathological Gambling: [redacted] atum

As described above, the ventral striat [redacted] portant contributions to motivated behaviors and reward processing [redacted] mplicated repeatedly in drug addiction (Knutson et al., 2001a,b; Chamber [redacted] Volkow and Li, 2004; Chambers et al., 2007). Individuals with pat [redacted] nbling have been found to show diminished activation of the ventral striatum [redacted] ated gambling and activation of this brain region correlated inversely with ga [redacted] ity amongst the subjects with pathological gambling (Reuter et al., 2005). [redacted] lata suggest that gambling urges in individuals with pathological gambl [redacted] ne cravings in individuals with cocaine dependence are similarly characteriz [redacted] ly diminished activation of the ventral striatum and orbitofrontal cortex (Po [redacted] Further research is needed to investigate the extent to which brain activati [redacted]

activation or response within the ventromedial prefrontal cortex was observed in the group with impaired impulse control as compared to the control comparison group (Hommer et al., 1997; Siever et al., 1999; New et al., 2002). No such imaging study to date has examined the role of serotonin in ventromedial prefrontal cortical functioning in individuals with pathological gambling.

Dopamine in Pathological Gambling

The ventral striatum is a target region for dopamine neurotransmission within the mesolimbic pathway, and dopamine function within the ventral striatum contributes to reward-ba

Parkinson's disease (one that involves degeneration of dopamine systems), an association between dopamine agonist treatment and impulse control behaviors including excessive gambling has been reported (Voon et al placebo and provided further support for a role for opioid systems in pathological gambling (Grant et al., 2006). However, preliminary results of a subsequent trial of nalmefene in pathological gambling did not generate positive findings (Biotie, 2007). A similar variability has been observed in studies of alcohol dependence (Krystal et al., 2001). Variability in study outcomes might be related to individual differences amongst subjects. For example, commonly occurring variants of the gene encoding the mu-opioid receptor have been associated with differential outcom variance and environmental factors for about one-third (Potenza et al., 2005). Genetic factors contributing to pathological gambling have been found to overlap with those for alcohol dependence (Slutske et al., 2000) and those for antisocial behaviors environmental contributions to these disorders suggests that specific life events can influence the development of these disorders and enactment of these behaviors, providing hope for prevention and treatment efforts.

Neurobiology of Ethics and Morality

Technological advances in imaging and genetics have provided exciting opportunities to investigate not only gambling, but also other behaviors and disorders with moral or ethical implications (Friedrich 2005). Results from these studies have are relevant to m contributions (Greene et al., 2004). However, this and similar models have been criticized in that they may not fully account for cultural influences on moral reasoning and decision-making (Moll et al., 2005a). Nonetheless, existing studies suggest that moral cognitions and behaviors involve a broad range of brain regions involved in cognitive and emotion processes in a social-context-dependent fashion, with different types of moral dilemmas activating preferentially different aspects of these neural circuits.

Consistent with this hypothesis, existing data differentially implicate specific brain regions in negotiating different moral processes. Amongst the brain regions most typically implicated in imaging paradigms probing moral cognition and behavior include cortical regions (e.g., ventromedial prefrontal cortex, lateral orbitofrontal cortex, anterior prefrontal cortex, dorsolateral prefrontal cortex, anterior temporal cortex, and superior temporal sulcus) and subcortical regions (amygdala, ventromedial hypothalamusha

2004). Ventromedial prefrontal and orbitofrontal cortex and amygdala are considered important contributors to social response reversal theory (commission of immoral behaviors related to difficulties in learning following negative outcomes), violent inhibition mechanism (deficienc embarrassment (Takahashi et al., 2004), indignation (Moll et al., 2005b) and guilt (Shin et al., 2000; Takahashi et al., 2004) have been associated with activations of these regions. However, this and competing models require further evaluation as to how they relate to moral judgment and behaviors in clinical and community samples.

Clinical samples may provide insight into aspects of social cognition and moral processing. For example, clinical groups characterized by antisocial behavior (e.g., sociopathy (Blair, 2003)) or excessive prosocial engagement (e.g., Williams Syndrome (St. George and Bellugi, 2000)) show abnormalities in the amygdala. Violent behaviors have been associated with orbitofrontal cortical abnormalities in antisocial personality disorder, although other brain regions (e.g., sensorimotor cortex) have also been implicated in this and other patient groups (Narayan et al., 2007). Damage to the bilateral temporal cortices or amygdala has been associated with social and appetitive disturbances (hypersexuality, placidity, and hyperorality and pica) (Hayman et al., 1998). The extent to which social and moral processing differs in individuals with pathological gambling as compared to those without warrants further investigation. Given that moral perceptions influence brain activations within reward processing regions (including striatum) in healthy subjects, it will be important to evaluate these processes as related to gambling behaviors.

Conclusions and Future Directions

Technical advances in genetics and brain imaging are providing important insight into brain processes related to moral reasoning and behavior.y 0 100 2607 0 TmW n /Cs1 cs 0 0 0 sc q 0 T

function underlying mental health and illness. Future research should examine more closely the relationships between these domains. The acquisition of knowledge about individual brain function with respect to moral and medical states raises questions about privacy and ethics (Friedrich, 2005). Although how best to use this information in various settings (e.g., legal, medical, and ethical venues) is currently a topic of discourse (Leshner, 2003; Friedrich, 2005; Buller, 2006; Eastman and Campbell, 2006), the knowledge should help further discussion about the roots of moral and immoral thoughts and behaviors. As applied to human health and disease, these advances offer hope to advance prevention and tret

Botvinick, M., Braver TS, Barch DM, Carter CS, Cohen JD (2001). "Conflict monitoring and cognitive control." Psycholog Rev **108**: 624-652.
Botvinick, M., Nystrom, LE, Fissell, K, Carter, CS, Cohen, JD (1999). "Conflict monitoring versus selection-for-action in anterior cingulate cortex." Nature **402**: 179-181.
Brewer, J. A. and M. N. Potenza (in press). "The neurobiology and genetics of impulse control disorders: relationships to drug addictions." Biochem Pharmacology.
Buller, T. (2006). "What can neuroscience contribute to ethics?" J Med Ethics **32**: 63-64.

Goldstein, R. Z., Volkow ND (2002). "Drug addiction and its underlying neurobiological basis: Neuroimaging evidence for the involvement of the frontal cortex." Am J Psychiatry

Knutson, B., Fong GW, Adams CM, Varner JL, Hommer D (2001b). "Dissociation of reward anticipation and outcome with event-related fMRI." Neuroreport **12**: 3683-3687.

Knutson, B., Fong GW, Bennett SM, Adams CM, Hommer D (2003). "A region of mesial prefrontal cortex tracks monetarily rewarding outcomes: characterization with rapid event-related fMRI." Neuroimage **18**: 263-272.

Knutson, B., Westdorp A, Kaiser E, Hommer D (2000). "FMRI visualization of brain activity during a monetary incentive delay task." Neuroimage **12**: 20-27.

Korn, D., Shaffer H. J. (1999). "Gambling and the health of the public: Adopting a public health perspective." J Gambling Stud **15**: 289-365.

Kreek, M. J., D. A. Nielsen, et al. (2005). "Genetic influences on impulsivity, risk-taking, stress responsivity and vulnerability to drug abuse and addiction 769.32001 re W n /2637 0 Tm ( )

Nordin, C., Eklundh, T (1998). "Tapping-time is longer in pathological male gamblers than in healthy male controls." J Psychiatr Res **32**: 421-422.
Oslin, D. W., W. Berrettini, et al. (2003). "A functional polymorphism of the mu-opioid receptor gene is associated with naltrexone response in alcohol-dependent patients." Neuropsychophamacology **28**: 1546-1552.
Petry, N. M. (2001a). "Pathological gamblers, with and without substance use disorders, discount delayed rewards at high rates." J Abnorm Psychology **110**: 482-487.
Petry, N., Casarella, T (1999). "Excessive discounting of delayed rewards in substance abusers with gambling probl

Shah, K. R., S. A. Eisen, et al. (2005). "Genetic studies of pathological gambling: A