Published in final edited form as:
Biol Psychiatry. 2012 November 15; 72(10): e25–e26. doi:10.1016/j.biopsych.2012.06.016.

Attending to Striatal Ups & Downs in Addictions

Iris M. Balodis, PhD[1,*], **Hedy Kober, PhD**[1], **Patrick D. Worhunsky, BSc**[1], **Michael C. Stevens, PhD**[2], **Godfrey D. Pearlson, MD, PhD**[1,2,3], and **Marc N. Potenza, MD, PhD**[1,3,4]

[1]Department of Psychiatry, Yale University School of Medicine, New Haven, CT, USA

[2]Institute of Living/Hartford Hospital & Olin Neuropsychiatry Research Center, Hartford, CT, USA

[3]Department of Neurobiology, Yale University School of Medicine, New Haven, CT, USA

[4]Child Study Center, Yale University School of Medicine, New Haven, CT, USA

Altered striatal responses during monetary reward anticipation have recently been reported in pathological gambling (PG). While van Holst and colleagues reported an increased response (1), Balodis and colleagues found a diminished response (2). Leyton and Vezina propose that these divergent results may relate to cue-specificity; in addicted populations addiction-related cues increase striatal activity, whereas in the absence of such cues, diminished striatal activity is observed. They suggest that the playing cards presented by van Holst and colleagues may be more familiar/salient to PG participants, whereas the predominance of text presented by Balodis and colleagues may account for the diminished striatal response. This explanation is complicated by several factors. First, PG samples in both studies were heterogeneous in their gambling preferences. Second, the Monetary Incentive Delay Task used by Balodis and colleagues included money symbols on each trial and references to currency, wins and losses – all of which might be considered addiction-related stimuli in PG.

Multiple factors may underlie different findings in the two studies, including sample differences (e.g. gender distribution, treatment-seeking status), analytic strategies (e.g. contrasts of magnitudes versus contrasts of wins relative to neutral conditions). In addition, features of reward processing and decision-making inherent in gambling-related activities and different across studies, (e.g. risk, uncertainty, probability, response preparation, guessing, choice) may influence ventral striatal recruitment. While these factors may impact findings, we propose that the two studies' results are not discrepant, but together provide insight into potential mechanisms of reward-processing alterations in PG. We posit that each study reports alterations in two different brain areas critical to reward processing: the ventral and the dorsal striatum.

[*]Corresponding Author: Iris M. Balodis, PhD, Yale University School of Medicine, 1 Church Street, Rm 731, New Haven, CT 06519, Tel: 203-737-2668, iris.balodis@yale.edu.

Disclosures

The authors report that they have no financial conflicts of interest with respect to the content of this manuscript. Dr Potenza has received financial support or compensation for the following: Dr Potenza consults for and is an advisor to Boehringer Ingelheim; has consulted for and has financial interests in Somaxon; has received research support from the National Institutes of Health, Veteran's Administration, Mohegan Sun Casino, the National Center for Responsible Gaming and its affiliated Institute for Research on Gambling Disorders, and Forest Laboratories, Psyadon, Ortho-McNeil, Oy-Control/Biotie and Glaxo-SmithKline pharmaceuticals; has participated in surveys, mailings or telephone consultations related to drug addiction, impulse control disorders or other health topics; has consulted for law offices and the federal public defender's office in issues related to impulse control disorders; provides clinical care in the Connecticut Department of Mental Health and Addiction Services Problem Gambling Services Program; has performed grant reviews for the National Institutes of Health and other agencies; has given academic lectures in grand rounds, CME events and other clinical or scientific venues; and has generated books or book chapters for publishers of mental health texts.

Human and animal studies demonstrate dissociable roles of these areas, specifically as they relate to reward processing and instrumental conditioning (3–9). The ventral striatum is implicated in reward-related anticipation, prediction, and motivation, whereas dorsal areas are instrumental in the motor demands and cognitive control associated with the acquisition of stimulus-response-reward associations (3,4). Also, as addictive behaviors become habitual, striatal involvement may shift from ventral to dorsal (10,11). Dorsal striatal-related networks are implicated in habitual behaviors (12), most studied in addictions for cue-driven drug use and craving (13). For example, relative to healthy controls, altered striatal activation is observed in abstinent cocaine-dependent individuals during reward receipt in a risk-taking game; these activation differences are greatest in the right dorsal caudate and correlate negatively with compulsivity and reward/punishment sensitivity (9).

Van Holst and colleagues administered a modified guessing task (14) where participants indicated their likelihood of winning/losing €5 versus €1 given 30% or 70% probabilities. Imaging contrasts between PG and control groups during the anticipatory phase of winning €5 versus €1 revealed greater bilateral dorsal striatum activity in PG participants. However, the corresponding Figure 1 and the abstract report this difference as the bilateral ventral striatum. The interpretation of the figure is complicated by the contrast-map threshold-level differing from that reported in the results section and being uncorrected for multiple comparisons. Similarly, the results report greater gain-related expected-value activity in the dorsal striatum in PG participants, yet the corresponding Figure 2 refers to ventral striatal differences using a different contrast-map threshold uncorrected for multiple comparisons.

Ventral and dorsal striatal boundaries are difficult to demarcate in humans relative to rats. Ventral/dorsal striatum confusion may partially be explained by the 18mm-diameter-sphere volume-of-interest centered on the ventral striatum used by van Holst and colleagues; a sphere of this size would likely also encompass dorsal striatum. The authors restricted their focus to subcortical and cortical areas. It could be informative to view task-related whole-brain activations and whole-brain between-group differences. Whole-brain information could be combined with smaller volumes-of-interest while keeping thresholding levels constant and maintaining corrections for multiple comparisons.

Nonetheless, between-group differences in gain-related expected-value activity reported by van Holst and colleagues in the dorsal striatum are important given this area's role in reward-related learning. The coordinates and contrast-maps correspond with the dorsal striatum, or specifically, the anterior caudate – a region signaling prediction error during instrumental conditioning (4). The dorsal striatum is also implicated in the perceived contingency between action and reinforcement; i.e., the extent to which an individual believes their performance determines the outcome (5,6). This is noteworthy as the authors describe disconnections between action and outcome by informing participants that their performance would not influence the win/loss outcome of each trial. Therefore, in this context, greater anticipatory dorsal-striatal activity suggests that PG participants may have increased susceptibility to form action-outcome associations. Interestingly, the dorsal-striatal contribution for stimulus-response reward-related activity occurs even when the actual algorithm is suboptimal, such as during the gambler's fallacy (15). Furthermore, the dorsal-striatal area involved in learning stimulus-response associations is that recruited during choice (3,4,15), suggesting an increased propensity in PG to learn arbitrary associations between situations and actions. In the van Holst et al. study, the PG group quickly recognized the greater magnitude of the €5 condition and performed the associated action (i.e. indicating their expectation). Rapid responding in PG relative to control participants supports this idea: mean reaction times were consistently more than 1 second faster for each condition type (although between-group differences were not statistically significant). Accelerated responding may reflect this stimulus-response association, or differences in

preparation and execution of motor responses, as these were also incorporated in the expectation phase in this study. These results suggest more rapid action-outcome association acquisition in PG, and together with the Balodis et al. results, indicate PG may involve greater inflexibility in modifying these associations (i.e., when ventral-striatal systems are hyporesponsive).

Functional roles of striatal subregions are dissociable and complex. Given the fundamental role of separate striatal subdivisions in different aspects of reward processing, careful attention should be given to anatomical distinctions. Dorsolateral and dorsomedial striatal regions are currently being further distinguished based on connectivity and function (16). To better understand anatomical and behavioral correlates of the striatum, we encourage a precise, nuanced approach in attending to striatal ups and downs.

Acknowledgments

Support was provided by the following Grants: National Institutes of Health grants R01-DA019039, P20-DA027844, P50-AA012870, R01-DA020908, R01-DA020709, R01-AA016599, RL1-AA017539, K12-DA00167, the Veterans Integrated Service Network 1 Mental Illness Research, Education, and Clinical Center (MIRECC), and a Center of Excellence in Gambling Research Grant from the National Center for Responsible Gaming and its Institute for Research on Gambling Disorders. The contents of the manuscript are solely the responsibility of the authors and do not necessarily represent the official views of the National Center for Responsible Gaming or the Institute for Research on Gambling Disorders or any of the other funding agencies.

References

1. van Holst RJ, Veltman DJ, Buchel C, van den Brink W, Goudriaan AE. Distorted expectancy coding in problem gambling: is the addictive in the anticipation? Biol Psychiatry. 2012; 71:741–748. [PubMed: 22342105]
2. Balodis IM, Kober H, Worhunsky PD, Stevens MC, Pearlson GD, Potenza MN. Diminished frontostriatal activity during processing of monetary rewards and losses in pathological gambling. Biol Psychiatry. 2012; 71:749–757. [PubMed: 22336565]
3. Atallah HE, Lopez-Paniagua D, Rudy JW, O'Reilly RC. Separate neural substrates for skill learning and performance in the ventral and dorsal striatum. Nat Neurosci. 2007; 10:126–131. [PubMed: 17187065]
4. O'Doherty J, Dayan P, Schultz J, Deichmann R, Friston K, Dolan RJ. Dissociable roles of ventral and dorsal striatum in instrumental conditioning. Science. 2004; 304:452–454. [PubMed: 15087550]
5. Tricomi EM, Delgado MR, Fiez JA. Modulation of caudate activity by action contingency. Neuron. 2004; 41:281–292. [PubMed: 14741108]
6. Haruno M, Kuroda T, Doya K, Toyama K, Kimura M, Samejima K, et al. A neural correlate of reward-based behavioral learning in caudate nucleus: a functional magnetic resonance imaging study of a stochastic decision task. J Neurosci. 2004; 24:1660–1665. [PubMed: 14973239]
7. Reading PJ, Dunnett SB, Robbins TW. Dissociable roles of the ventral, medial and lateral striatum on the acquisition and performance of a complex visual stimulus-response habit. Behav Brain Res. 1991; 45:147–161. [PubMed: 1789923]
8. Balleine BW, Delgado MR, Hikosaka O. The role of the dorsal striatum in reward and decision-making. J Neurosci. 2007; 27:8161–8165. [PubMed: 17670959]
9. Hyatt CJ, Assaf M, Muska CE, Rosen RI, Thomas AD, Johnson MR, et al. Reward-related dorsal striatal activity differences between former and current cocaine dependent individuals during an interactive competitive game. PLoS One. 2012; 7:e34917. [PubMed: 22606228]
10. Porrino LJ, Smith HR, Nader MA, Beveridge TJ. The effects of cocaine: a shifting target over the course of addiction. Prog Neuropsychopharmacol Biol Psychiatry. 2007; 31:1593–1600. [PubMed: 17900777]

11. Takahashi Y, Roesch MR, Stalnaker TA, Schoenbaum G. Cocaine exposure shifts the balance of associative encoding from ventral to dorsolateral striatum. Front Integr Neurosci. 2007; 1:11. [PubMed: 18958239]

12. Yin HH, Knowlton BJ. The role of the basal ganglia in habit formation. Nat Rev Neurosci. 2006; 7:464–476. [PubMed: 16715055]

13. Everitt BJ, Robbins TW. Neural systems of reinforcement for drug addiction: from actions to habits to compulsion. Nat Neurosci. 2005; 8:1481–1489. [PubMed: 16251991]

14. Yacubian J, Glascher J, Schroeder K, Sommer T, Braus DF, Buchel C. Dissociable systems for gain- and loss-related value predictions and errors of prediction in the human brain. J Neurosci. 2006; 26:9530–9537. [PubMed: 16971537]

15. Jessup RK, O'Doherty JP. Human dorsal striatal activity during choice discriminates reinforcement learning behavior from the gambler's fallacy. J Neurosci. 2011; 31:6296–6304. [PubMed: 21525269]

16. van der Meer M, Kurth-Nelson Z, Redish AD. Information Processing in Decision-Making Systems. Neuroscientist. 2012