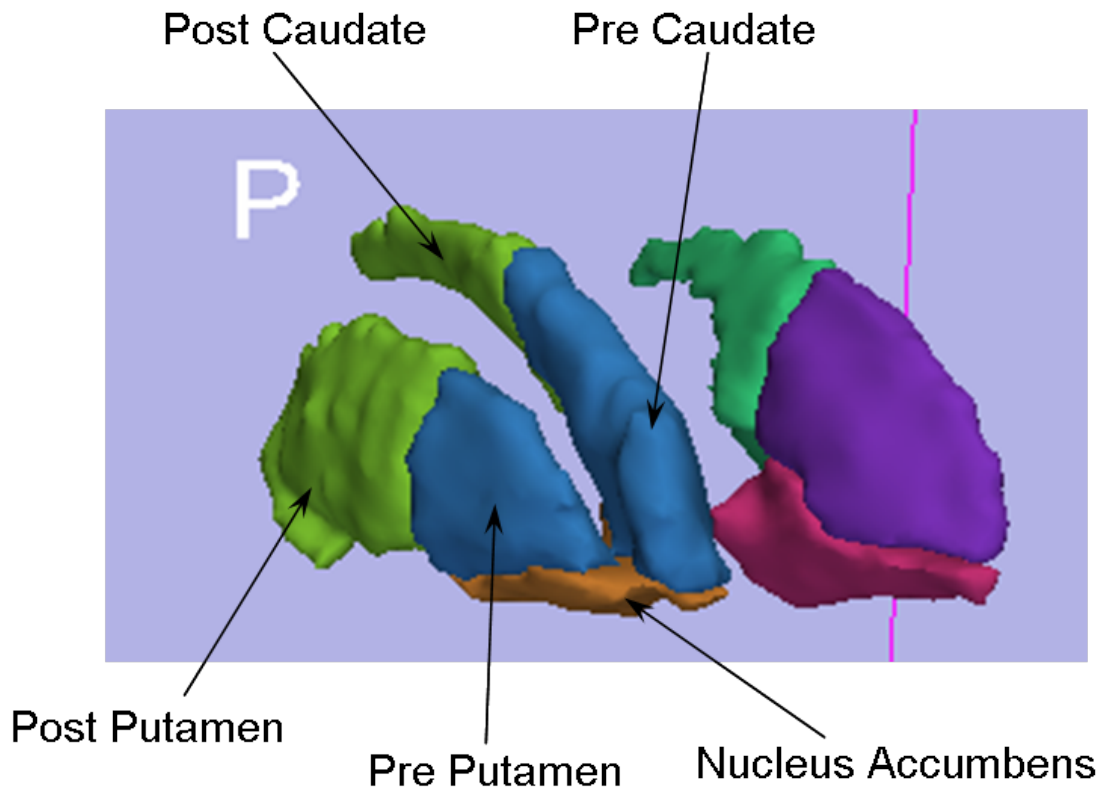


EC 490

Lecture 13: Functionally parsing the striatum

1. This lecture is about functionally discriminating *within* the striatum. Is there a reason a neuroeconomist should be interested in this? (Consider: the macroeconomist doesn't care about which room in the Treasury Department is the one where the final national budget is consolidated.)
2. But, yes, there is a reason. Spatial discrimination is one basic way of determining which functions are partly or wholly independent of one another. This is often unclear given even the most carefully elicited behavioral evidence.



3. We further divide NAcc into 'shell' and 'core' areas.
4. A less fine-grained breakdown of the striatum divides it into ventral and dorsal regions. Ventral striatum includes NAcc and (confusingly) the lower parts of the putamen and caudate. Dorsal striatum incorporates the upper parts of the putamen and caudate.
5. Different parts of striatum project to different parts of frontal cortex, which then project back to them, thus creating loops. Some connecting circuits (using neurotransmitter GABA) are inhibitory, while others (Glutamate and Serotonin) are excitatory. Excitatory projections from subcortical regions, including anterior cingulate and amygdala, reach into NAcc.
6. Within striatum, ventral tegmental area projects to ventral striatum and pars compacta of substantia nigra projects to dorsal striatum.
7. Lesion and disease studies historically suggested that impaired ventral striatal functioning compromises motivations, while impaired dorsal striatal functioning compromises motor behavior. (Parkinson's disease first strikes at dorsal striatal processing.)
8. Knutson *et al* first report on microdialysis studies of rats. Eating and drinking increase dopamine release in NAcc and dorsal caudate. This effect is stronger when food is highly palatable. Sex has a similar, stronger, effect. However, microdialysis probes can't distinguish response to anticipation from response to consumption.
9. Striatal dopamine response is also observed when rats are stressed (e.g., by shock or restraint). But there is some evidence that this reflects anticipation of relief from the

- termination of the stress. The effect is strongest in animals with experience of the relevant stressors. They, unlike naïve animals, have learned that the stress always ends after a few seconds or minutes.
10. Knutson *et al* distinguish between ‘tonic’ and ‘phasic’ dopamine changes. A ‘phasic’ change is a brief irruption at a specific location or receptor site. A ‘tonic’ change is a change in general dopamine levels in the whole circuit, which may be highly persistent. Microdialysis detects tonic changes. For picking up phasic changes (in rats), one can use voltammetry, in which an electrical potential is used to oxidize groups of neurons.
 11. Using this technique, phasic dopamine increases were observed in NAcc shell when rats (i) entered novel environments, (ii) prepared to press levers for food, (iii) saw receptive females, (iv) smelled bedding from females in estrus, and (v) met new rats. These levels fell when the food rewards were received and while they were being consumed. Dorsal striatum has so far not been examined by this method under similar circumstances. Nor has it been used to monitor dopamine in striatum on presentation of aversive stimuli.
 12. Positron emission tomography (PET), though more invasive than fMRI (radioactive oxygen or glucose is injected into participants), can be used with human subjects. In subjects playing videogames, PET scanning observed phasic dopamine increases at D2 receptors in NAcc and caudate when subjects earned points. Dopamine changes in the same areas were *not* observed when subjects experienced losses.
 13. Unlike PET scanning, fMRI scanning can’t detect specific neurochemical changes. It’s also challenging to use it to study striatum, because bloodflow in the palette interferes

with the BOLD signal from the brain. On the other hand, fMRI has far greater spatial and temporal precision than PET, and is non-invasive.

14. In an early fMRI study, Knutson *et al* showed that monetary incentives in tasks increased striatal activation relative to what was observed in identical tasks without the incentives. This study didn't attempt to distinguish between anticipation and receipt of monetary rewards.
15. Elliott *et al* then scanned subjects engaged in gambling. They found that wins were correlated with activity in putamen and midbrain, while losses were correlated with activity in medial temporal lobe. Delgado *et al* repeated the experiment but controlled for anticipation. They found that gain outcomes were correlated with higher caudate activation relative to loss and neutral outcomes. Breiter *et al* obtained results consistent with but extending these previous ones. In their gambling task experiment, both anticipated and received rewards activated NAcc, while loss-related activity occurred outside the striatum. Knutson *et al* focused directly on anticipated gains and losses, and their results *partly* matched Breiter's: they observed enhanced NAcc and medial caudate activity on anticipation of gains, with NAcc falling out of the picture – and an extra-striatal area, thalamus, entering it – on anticipated losses. They also observed NAcc activation when subjects were merely reminded of money.
16. Since these baseline-setting studies, the real neuroeconomic work – the attempt to isolate decision variables from striatal observation – has been on. Knutson *et al* reported that ventral striatum was sensitive to expected gain magnitude, while MPFC responded to expected gain probability. Several studies suggested that ventral striatum in fact responds to both variables, but is positively correlated

with magnitude while being complexly correlated with probability, peaking at intermediate ranges. Some other studies agreed with the result on magnitude, but found a simple positive correlation between VS activity and probability. The authors of the chapter suggest that signal coding for probability is phasic, and thus susceptible to being detected at different points in its time course from one study to another, while all studies pick up a tonic change related to magnitude. Another possibility is that, since low-probability conditions in gambling tasks necessarily involve higher loss frequencies, the losses in these conditions might induce interference effects from anticipation of such losses.

17. There is a lively and important controversy now going on – which we'll revisit later – concerning the influence of reward delay. McClure *et al* found higher activation in VS, MPFC and posterior cingulate when subjects chose between one immediate and one delayed reward than when they chose between two delayed rewards. Kable and Glimcher, however, observed results directly inconsistent with this: they found no brain activity that suggested a different delay function when one option in a choice delivered reward immediately. (All activity they observed best fit a one-parameter hyperbolic function.)
18. There is emerging evidence that caudate activation is sensitive to relative as well as to absolute reward magnitudes.
19. An important question is whether striatal responses to incentives are coding for gains themselves or for learning of actions that yield gains. In the latter case, activation should attenuate as good actions become more habitual. Some recent studies suggest that although both of these representations occur in striatum, caudate activity responds to learning

opportunities while putamen keeps the books.

20. What do we find when, guided by hypotheses just considered, we manipulate non-human subjects' brains and try to predict their behavior? Infusing dopamine-releasing agents into rat VS increases their tendency to approach stimuli that have previously predicted rewards, and triggers general seeking behaviors. Stimulating monkey caudate while subjects process rewards speeds up their learning of cues and actions associated with the reward in question.
21. The latter result is consistent with fMRI findings in humans to the effect that VS activation associated with monetary reward is in turn associated with better recall of predictive cues. The authors say that this suggests a role for striatum in memory. In one trivial way it indeed does: everything in the brain is memory. However, it's not at all clear that this three-term correlation adds any knowledge beyond what we have from the association between VS activity and reward. Had correlation between reward and recall *not* been observed, after all, we would be very surprised, and this surprise would be independent of anything we had or hadn't learned about striatal activity. Evidence that reward cue learning activates hippocampus is more informative, since hippocampus is independently associated with *long-term* memory formation.
22. In humans choosing investments under fMRI scanning, VS activation just before choice predicted choice of riskier options (after controlling for variables such as wealth), including under circumstances in which EV optimization counter-predicted the choice. Knutson *et al* interpret this as evidence that VS is insensitive to opportunity cost. I think this inference is (extremely) hasty, because the experiment didn't control for concavity of subjects' utility functions or

- their attitudes to risk.
23. More directly interesting is a simple result from Knutson *et al* in which VS activity in subjects deciding whether to purchase consumer products was a better predictor of their choices than were their subjective preference reports.
 24. In another experiment, VS activation levels predicted the extent to which heterosexual male subjects would prefer risky to less risky gambles after observing sexy pictures.
 25. Finally, several experiments have focused on the relationship between striatal activity and social decisions. Caudate activation has been associated with observation of reciprocated trust in PDs and subjects' dispositions to invest in partners who had cooperated with them in TGs. Delgado *et al* found higher VS activation when human subjects observed behavior of subjects they'd been led to believe had good reputations than when they observed behavior of subjects about whom they'd been fed negative or neutral information.
 26. Knutson *et al* suggest – rightly, I think – that the most general and important conclusion we should take away from these studies is that in the brain – at least at a certain scale of analysis – gains and losses aren't coded as opposites of one another along a single representational domain, but are tracked by separate systems.
 27. Quite important to work we'll examine shortly, anticipation and receipt of reward also appear to be separately encoded, in different (overlapping?) parts of striatum. Anticipation appears to mainly be represented ventrally, while outcomes are mainly represented dorsally.

