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Press Room, Nov. 12–16: (202) 249-4080

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## **NEW DISCOVERIES ABOUT HUMAN RISK AVERSION AND DECISION-MAKING**

*Research helps explain ways the brain maximizes reward and minimizes loss*

**Washington** — What makes us decide to play it safe or take a risk? Scientists presented research today identifying regions and functions of the brain involved in such decisions to provide fresh insights into how humans explore the unknown. These findings also add to a relatively new area of inquiry — neuroeconomics and the study of economic behavior. The research was presented at Neuroscience 2011, the Society for Neuroscience’s annual meeting and the world’s largest source of emerging news about brain science and health.

Specifically, today’s new findings show that:

- The brain chemical serotonin may be involved in risky decision-making. Researchers found that when certain serotonin receptors are blocked, people are less likely to take a gambling risk (Julian Macoveanu, PhD, abstract 931.10, see summary attached).
- Given multiple opportunities to choose, people seek out unfamiliar options over known outcomes (Robert Wilson, PhD, abstract 830.13, see summary attached).

Other recent findings discussed show that:

- Brain cells in the orbitofrontal cortex of the monkey brain assign values to different goods. The activity of these cells adapts to the range of values presented and is independent of the value of alternative options (Camillo Padoa-Schioppa, PhD, see attached speaker’s summary).
- The brain circuit connecting the cortex and basal ganglia is involved in “deciding” which behavior to pursue. Studying this circuit yields new information about emotional decision-making and insights into certain neurological disorders, like obsessive-compulsive-spectrum disorders and addiction (Ann Graybiel, PhD, see attached speaker’s summary).

“These studies help deepen our understanding of the highly complex mechanisms involved in decision-making,” said press conference moderator Michael Platt, PhD, of Duke University, an expert in cognitive behavior and the brain. “Such research is not only helping us understand how and why we make the choices we do, but it also may lead to more effective interventions for some of the many brain disorders that are characterized by poor decision-making.”

This research was supported by national funding agencies, such as the National Institutes of Health, as well as private and philanthropic organizations.

### **Related Presentations:**

Dialogues Between Neuroscience and Society: **Animal Spirits: How Human Behavior Drives the Economy**  
Saturday, Nov. 12, 11 a.m.–1 p.m., Hall D

Presidential Special Lecture: **The Basal Ganglia: Binding Values to Action**  
Sunday, Nov. 13, 5:15–6:25 p.m., Hall D

Special Lecture: **The Pluses and Minuses of Optimal Action Selection**  
Tuesday, Nov. 15, 1–2:10 p.m., Hall D

## Abstract 931.10 Summary

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### **Blocking Serotonin Reduces Risky Gambling Behavior** *Drug also reduces brain activity, but only after losses, not wins*

A drug that blocks serotonin, a brain chemical important in mood, makes study participants less likely to make risky gambling decisions, according to new research. The drug also reduced activity in frontal brain regions, but only after participants lost a gamble they thought they should have won. The findings were presented at Neuroscience 2011, the Society for Neuroscience's annual meeting and the world's largest source of emerging news about brain science and health.

Researchers, led by Julian Macoveanu, PhD, of the Danish Research Centre for Magnetic Resonance, asked 20 healthy volunteers to perform a gambling task. Participants were told to maximize their net gain by choosing between options associated with different odds to win — all while undergoing a functional magnetic resonance imaging (fMRI) scan.

To study the effects of serotonin on decision-making, volunteers received infusions of ketanserin, a drug that blocks certain serotonin receptors, during one of the sessions. After receiving ketanserin, participants were less likely to take risks during the gambling task. They also exhibited less activity in frontal regions of the cortex. But these changes were observed only when the volunteers were evaluating risk after experiencing an unfair loss — that is, after they had chosen a low-risk option in the gambling task but still lost.

“When gambling, people tend to be more sensitive to potential losses than gains of similar amounts, indicating that loss avoidance plays a major role when we make risky decisions,” said Macoveanu. “Our findings may have clinical significance because patients with mood and anxiety disorders, some of which are associated with dysfunctions in serotonin transmission, often overemphasize the impact of negative outcomes,” he said.

Research was supported by the Lundbeck Foundation for the Center for Integrated Molecular Brain Imaging.

Scientific Presentation: Wednesday, Nov. 16, 2–3 p.m., Halls A–C

931.10, Playing it safe and being punished for it: 5-HT<sub>2A</sub> signaling and risk aversion

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**TECHNICAL ABSTRACT:** Would you like to play it safe or take a risk? During risky decision-making, people seem to be more sensitive to potential losses than gains of similar amounts, indicating that loss avoidance plays a major role when we make risky decisions. It has been proposed that serotonin (5-HT) plays a critical role in loss avoidance and processing negative outcomes. Further, 5-HT<sub>2A</sub> receptor antagonists markedly attenuate increases in stimulated striatal and cortical dopamine release. In this study, we used pharmacological fMRI to examine how 5-HT<sub>2A</sub> related signaling is involved in processing negative outcomes produced by loss-avoiding decisions. Twenty healthy subjects (age range: 20 to 40), performed a gambling task during two fMRI sessions, one with no drug or and one after intravenous infusion of the 5-HT<sub>2A</sub> receptor blocker ketanserin. The gambling task required participants to maximize their net gain by choosing between low risk options with low potential outcome and high risk options with high potential outcome. The task parametrically modulated the probability of winning and associated outcome while keeping the size of the potential losses constant. Data analysis focused on ketanserin induced changes in neural processing of negative outcomes and possible links to risk avoidant behavior. Analysis of the choice distributions across the risk levels revealed that participants became more loss avoidant after blocking the 5-HT<sub>2A</sub> receptors. The behavioral shift towards fewer high risk choices following ketanserin administration correlated with activity in right dorsomedial prefrontal cortex. Ketanserin reduced loss-related activity in orbitofrontal and ventro lateral prefrontal cortex following low risk choices as compared to medium and high risk choices. The data suggest that blocking the 5-HT<sub>2A</sub> receptors increases the impact of unexpected negative outcomes following a safe choice on the decision process resulting in a more risk avoiding behavior compared to normal conditions.

## Abstract 830.13 Summary

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### **People Seek Ambiguity If Given Multiple Opportunities To Choose**

*Findings refute belief that people are averse to uncertainty*

When given more than a single opportunity to choose between two outcomes, people are more likely to select the unknown, according to new research presented at Neuroscience 2011, the Society for Neuroscience's annual meeting and the world's largest source of emerging news about brain science and health.

The findings diverge from traditional accounts of ambiguity aversion, the idea that people prefer known to unknown risks. "These results suggest that the grass is greener on the other side, but only when you have multiple opportunities to cross the fence," said lead author Robert Wilson, PhD, of Princeton University.

For the study, Wilson and his colleagues designed an experiment using slot machines that mimicked a very common decision: when you're at a restaurant, should you order a meal you've had before and liked (ambiguity-averting behavior) or should you try something new (ambiguity-seeking behavior)?

Most studies of ambiguity behaviors offer participants only a single choice. In the current study, the researchers offered people multiple opportunities to choose between two options; choices were randomly assigned point values to encourage "sampling." Under these circumstances, people, on average, value-rated an option about 15 percent higher when it was unknown.

However, when given only one opportunity to choose between a known and an unknown option, this "ambiguity bonus" went away, and the participants had a mild preference for the better-known option. The data suggest that rather than having an aversion to uncertainty, people adjust their attitudes toward uncertainty according to the demands of the task.

"Our results have important implications for the understanding of how humans explore the unknown, whether that's looking for a mate, buying a new car, or simply searching for a greener patch of grass," said Wilson.

Research was supported by the J. Insley Blair Pyne Fund Award.

Scientific Presentation: Wednesday, Nov. 16, 8–9 a.m., Halls A–C

830.13, Why the grass is greener on the other side: Behavioral evidence for an ambiguity bonus in human exploratory decision-making

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**TECHNICAL ABSTRACT:** When you go to a restaurant, do you always order the same thing or do you try something new? Going with an old favorite guarantees a happy meal, but you might miss out on something better unless you're willing to explore. The decision between choosing what you know and trying something different is called the Exploration-Exploitation problem.

Theoretical accounts suggest that explore-exploit decisions should be driven by both the expected value and the ambiguity associated with each option. When tractable, optimal strategies assign value to both of these factors, such that an ideal agent can choose an option with lower expected value when its ambiguity is high. Although the effects of expected value on human decision making are well understood, the effects of ambiguity have received relatively little attention and the optimal model's proscribed behavior seems counter to decades of research showing that humans are averse to ambiguity. We believe that this may reflect the fact that tests of ambiguity aversion usually involve a single choice, without the opportunity to reduce ambiguity by sampling. When given this opportunity, we predicted people would actually become ambiguity seeking.

We designed a task to test this prediction and tease apart the contributions of expected value and ambiguity in sequential decision making. In our "forced-play bandits task", subjects played a series of games lasting ten trials each. On each trial subjects selected one of two options which paid out points probabilistically. Subjects were instructed to maximize the number of points earned over the experiment and thus faced the explore-exploit dilemma afresh in each new game. In the first four trials of each game participants were forced to select one option. By varying the number of times a given option was chosen during these forced plays, we were able to manipulate the level of ambiguity subjects faced when making their first free decision. Specifically, we used the forced play trials to set up

two different ambiguity conditions: an “equal” condition, in which both options were played twice; and a “different” condition, in which one option was played once and the other three times.

We analyzed the data on the first free play trial by computing psychometric choice curves for each ambiguity condition as a function of the difference in means for the two options. In most subjects we found a significant bias in the “different” condition that was consistent with the ambiguity seeking behavior of the optimal model.

These results confirm our initial hypothesis and suggest that, rather than having a blanket aversion to ambiguity, humans modulate their attitudes to ambiguity according to the demands of the task.

## Speaker's Summary

**Speaker: Camillo Padoa-Schioppa, PhD**  
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### **Menu Invariance And Range Adaptation In Orbitofrontal And Anterior Cingulate Cortex (114.04)**

Minisymposium: Context-Dependent Neural Representations of Value: Gain Control, Adaptation, and Efficient Coding

Sunday, Nov. 13, 9:15–9:35 a.m., Washington, D.C. Convention Center, Room 207B

Economic choice is the behavior observed when individuals make choices solely based on subjective preferences — for example out of a restaurant menu. During economic choice, subjective values are assigned to the available options, and a decision is made by comparing values. The current view is that choices may be based on values computed in the orbitofrontal cortex (OFC). A fundamental question in the emerging field of Neuroeconomics is how the encoding of value depends on the behavioral context of choice. Importantly, there are at least two ways in which the context may vary. First, any given good may be offered against a variety of other goods. For example, a person in a gelateria may choose between chocolate and nocciola or, alternatively, between chocolate and pistachio. Such changes are referred to as changes of "menu." Second, the range of values available in different contexts can vary substantially. For example, the same person may choose between gelato cones (worth a few dollars) and other times between houses for sale (worth many thousands of dollars). In a series of studies, we examined how the encoding of value depends on the menu and on the value range. In our experiments, monkeys chose between different juices offered in variable amounts and subjective values were inferred from their choices. We found that the representation of value in the OFC was both menu invariant and range adapting. In other words, the activity of neurons encoding the value of one particular good did not depend on the good offered as an alternative (menu invariance). At the same time, the activity of all value-encoding neurons adapted to the range of values available in any behavioral condition. Range adaptation was also observed in the anterior cingulate cortex (ACC), where we found two separate representations of subjective value.

The theoretical implications of these results are far-reaching. On the one hand, menu invariance essentially implies that preferences are transitive. (Preference transitivity means that a person who prefers chocolate to nocciola and nocciola to pistachio also prefers chocolate to pistachio). Notably, preference transitivity is a hallmark of rational decision making and a fundamental assumption in economic theory. This key trait of choice behavior appears to be rooted in the OFC. On the other hand, range adaptation implies a computationally efficient representation. In essence, a given range of neural activity can represent different ranges of values at different times. This trait guarantees that the same individual can choose effectively in different behavioral contexts.

Part of this work has been published (Padoa-Schioppa and Assad, *Nature Neurosci* 2008; Padoa-Schioppa, *J Neurosci* 2009) and part is presented at this meeting for the first time. Traditionally, the object of economic theory and experimental psychology, economic choice, has recently become a lively focus of research in systems neuroscience. In addition to its intrinsic interest, economic choice is also relevant to numerous clinical conditions such as major depression, frontotemporal dementia and drug addiction. Previous work showed that OFC lesions specifically impair choice behavior. Furthermore, neurons in OFC encode the values subjects assign to different goods while choosing. For example, when a monkey chooses between grape juice and apple juice, some neurons in OFC represent the value of one of the two juices (offer value), other neurons represent the value of the chosen juice (chosen value), and other neurons represent the identity of the chosen juice (chosen juice). Importantly, the representation of value in OFC is abstract — it does not depend on the action executed by the animal to implement its choice.

## Speaker's Summary

**Speaker: Ann Graybiel, PhD**  
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Featured Lecture: **The Basal Ganglia: Binding Values to Action** (214)  
Sunday, Nov. 13, 5:15–6:25 p.m., Washington, D.C. Convention Center, Hall D

Value estimates are embedded in much of what we choose to think and do, and representations of value are widely distributed in the brain. How these value estimates are set is key to understanding the neural representation of thought and action. Yet, although value is sometimes mindfully attended, at other times value is ignored or overridden in our daily behavior. When we act out of “habit,” we can perform sequences of behavior that initially are clearly directed by this value-monitoring function of the brain; but in other instances, including in the extreme routines characteristic of obsessive-compulsive-spectrum disorders and addiction, our behaviors seem to occur regardless of the positive or negative value of the behaviors. In yet other disorders, value estimates seem too negative or too positive, as though state-changes in the evaluation system have occurred. This lecture will focus on new experimental findings about how cortico-basal ganglia circuits operate as positive and negative expected outcome values are learned, and as the transitions from clearly value-driven to semi-automatic, habitual behaviors occur. Recordings of neural activity in the striatum and neo-cortex of animals suggest that there is large-scale plasticity in cortico-basal ganglia circuits as habits are acquired, and that this plasticity involves not only changing patterns of spike activity, but also changing oscillatory patterns detectable in local field potential activity and changes in neurotransmitter signaling and gene expression. Strikingly, the circuits can be quite flexible or quite fixed in their signaling properties; these contrasts yield insights into the transition states between intentional and habitual behavior. It is likely that many of these changes reflect epigenetic modulation of circuits interconnecting elements in extended cortico-basal ganglia circuits. With the development of optogenetic methods, the dynamics of cortico-basal ganglia circuits can be probed along with the monitoring of behavior and neural activity. These combinations of methods are yielding a new view of the transitions in behavior that take us from behavioral flexibility to behavioral fixity. These methods are also yielding new views of emotional decision-making. Remarkably, the same circuits that operate in the transition from deliberative to habitual behavior are implicated in a range of neurologic and neuropsychiatric disorders. Our goal is to uncover mechanisms of action of these circuits that will yield critical insights into the neurologic and neuropsychiatric disorders that emerge as a result of dysfunction in cortico-basal ganglia circuits.