Embargoed until November 18, 10 a.m. ET **Contacts:** **Sara Harris, (202) 962-4087**
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NEW STUDIES IDENTIFY THE NEURAL BASIS OF DECISION-MAKING AND HOW IT IS AFFECTED BY LACK OF SLEEP

Findings add to growing understanding of how the brain processes components of thousands of daily decisions

Washington, DC — New studies released today decode the brain mechanisms involved in changing one's mind and sticking to one's guns, and show how this process is affected by sleep deprivation. These studies were discussed along with other recently released findings about how humans and other animals make thousands of daily decisions, from simple choices about where to gaze, to social judgment about morality. The research was presented at Neuroscience 2008, the annual meeting of the Society for Neuroscience and the world's largest source of emerging news about brain science and health.

The new findings show that:

- Twenty-four hours without sleep made human subjects more likely to take risks — heightening the allure of expected gains through activation of the striatum and dulling the brain's response to loss in a brain region called the insular cortex (Vinod Venkatraman, abstract 715.8, see attached summary).
- Neurons involved in decision-making also signal choice confidence in monkeys. Monkeys and humans alike make decisions when evidence accumulates to a critical threshold level, but may change their minds as additional information is processed (Michael Shadlen, see attached speaker's summary).

Related recent findings being discussed at the press conference:

- The orbitofrontal cortex — which plays a role in judgment — is vital in helping us understand when results differ from expectations, the first step toward modifying behavior (see attached speaker's summary).
- Two different brain structures are involved when expectations are undermined or exceeded. Neurons in a deep brain structure called the habenula respond to coming up short and they contact and inhibit their counterparts, dopaminergic neurons in the basal ganglia that respond to windfalls (see attached speaker's summary).
- The development of a moral brain in humans is very much embedded in social relationships. The process begins with neurochemicals that signal safety and facilitate affiliative relationships, and may influence decisions through a problem-solving process in neural networks. This view contrasts with previous thinking focusing on morality as a function of our capacity to reason and re-emphasizes the importance of social skills as a moral shaper (see attached speaker's summary).

"The brain is the foundation of the mind and hence, the key organ controlling how humans and other animals make practical and moral decisions," said press conference moderator Emery N. Brown, MD, PhD, from Massachusetts Institute of Technology and Massachusetts General Hospital. "Researchers continue to learn how the brain draws on memory, emotion, and other information to make predictions and to drive action."

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Related Presentations:

Symposium: **Habenula: Crossroad Between the Basal Ganglia and the Limbic System**
Wednesday, November 19, 8:30–11 a.m., Washington Convention Center, Ballroom B

David Kopf Lecture on Neuroethics: **How Do Brains Navigate Their Social/Moral Worlds?**
Monday, November 17, 10–11 a.m., Washington Convention Center, Hall D

Special Lecture: **The Neurobiology of Decision-Making: A Window on Cognition**
Sunday, November 16, 8:30–9:30 a.m., Washington Convention Center, Hall D

Special Lecture: **A New Perspective on the Role of Orbitofrontal Cortex in Decision-Making, Judgment, and Adaptive Behavior**
Monday, November 17, 8:30–9:30 a.m., Washington Convention Center, Hall D

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Abstract 715.8 Summary

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Study Finds Sleep Deprivation Increases Risky Decision-Making

Brain scan shows how staying up all night turns gamblers into greater risk-takers

Washington, DC — The odds are against people who gamble into the night, according to a new study from Duke University in Durham, N.C., and the Duke-NUS Graduate Medical School in Singapore. Researchers have found that being sleep-deprived not only makes us sleepier and less attentive, it also increases our chances of tossing caution — and our hard-earned money — to the wind. The study was presented at Neuroscience 2008, the annual meeting of the Society for Neuroscience and the world's largest source of emerging news about brain science and health.

"The advent of online gambling and 24-hour casinos have given us unprecedented opportunities for gambling into the night," said Vinod Venkatraman, the study's lead author. "But it might be better for us to catch some sleep rather than staying up late gambling. We're fighting more than just the unfavorable odds of the gambling machines."

In an earlier study, Venkatraman and his colleagues reported that sleep-deprived people tend to overestimate their chances of winning when placed in a gambling situation. In the current study, the researchers sought to better understand how going without sleep for 24 hours changes people's preferences and strategies for risky decision-making.

Twenty-nine young adults (14 women and 15 men, with a mean age of 22.3 years) were recruited for the study. Their brains were scanned while they played a gambling game that resulted in different outcomes based on different risk strategies. The testing was done twice: following a night of normal sleep and after 24 hours of no sleep.

When well rested, the volunteers favored a loss-averse gambling strategy, one in which avoiding losses was preferred to acquiring gains. But when sleep deprived, the same individuals demonstrated a greater preference for a gain-seeking strategy, one in which the possibility of big gains trumped concern over big losses.

The study also found striking differences in neural responses to how much money was lost or gained. When the volunteers were sleep deprived, following losses their brains showed less activation in the insular cortex, a region typically associated with negative mood and emotions. They also displayed greater activation in the striatum following gains. The striatum contains many receptors for dopamine, a chemical that plays a key role in reinforcing rewarding behavior and that is important in addiction.

"These findings argue for a simple conclusion about sleep deprivation: It promotes risk-seeking behavior by increasing neural responses to anticipated gains while diminishing responses to losses," Venkatraman said.

The research was supported by the Defense Science and Technology Agency of Singapore, the National Medical Research Council of Singapore, and the U.S. National Institute of Mental Health.

Scientific presentation: Wednesday, November 19, 9:45–10 a.m., Washington Convention Center, Room 147B

715.8, Sleep deprivation modulates risky decision -making strategies

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TECHNICAL ABSTRACT: Sleep deprivation (SD) enhances risk-seeking behavior by elevating expectation of high gains and attenuating the emotional impact of losses. Using a novel incentive-compatible decision-making task that involved sets of five outcomes ranging from large monetary losses to large monetary gains (Fig. 1), we sought to explore the neural bases of the effects of sleep deprivation on decision making strategies involving risk. Critically, the task was constructed so that subjects chose between two types of options: overall probability focused (OPF) and extreme value focused (XVF). Using the OPF strategy increased the overall chance of winning money compared to losing money, whereas using the XVF strategy either increased the magnitude of the extreme monetary gain (XVF-gain) or reduced the magnitude of the extreme monetary loss (XVF-loss). Prior results using normal healthy adults indicate individual differences in the preference for these strategies. Activation in inferior parietal lobule and dorsolateral PFC predicted OPF choices whereas activation in right anterior insula and vmPFC predicted XVF-loss and XVF-gain choices respectively.

Twenty-nine volunteers (14 females, mean age = 22.3 years) underwent functional neuroimaging in two sessions, following a night of normal sleep (rested wakefulness; RW) and after 24 h of sleep deprivation. We found a significant interaction between decision-making strategies and states ($F(1,28) = 6.702$, $p = 0.015$): SD participants showed greater preference for XVF-gain and reduced preference for XVF-loss choices. These findings are consistent with an increase in risk-seeking behavior following SD. FMRI analysis elucidated the neural mechanisms associated with these shifts in strategy across states and also provided insight into differences in sensitivity to monetary outcomes.

Speaker's Summary

Speaker: Michael Shadlen, MD PhD **(206) 616-4630**
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Seattle, Wash.

Special Lecture: **The Neurobiology of Decision-Making: A Window on Cognition**
Monday, November 16, 8:30–9:30 a.m., Washington Convention Center, Hall D

An emerging body of experimental results reveals how the brain makes decisions. We discovered neurons in association cortex (parietal & prefrontal lobes) that form a decision by accumulating relevant information from other brain areas — information that they construe as evidence in favor of a hypothesis and against its alternative(s). They signal the level of evidence through the rate of electrical impulses (spike rate). A decision is made when the rate reaches a critical level, or threshold.

These neurons perform the same mathematical operations that codebreakers performed in WWII to decipher the German Enigma code. More importantly, the neurobiology of decision-making opens a window on advanced cognitive operations at the refined microscopic level of single-cell physiology and thus promises to lay the foundation for understanding psychiatric and neurological disorders affecting higher mental function.

While much is known about how the brain senses information and moves body parts, less is known about what lies between sensation and action. Even simple decisions necessitate a level of complexity, contingency and freedom that challenge the view of mind as a machine connecting inputs and outputs. How does the brain weigh evidence in favor of competing alternatives? When should deliberation cease and give way to a choice? How does the brain negotiate the tradeoff between accuracy and speed? Why are we more confident in some choices than in others? Why do we change our mind?

Our recent experiments address these questions by measuring the electrical signals from neurons in the brains of monkeys as they ponder video evidence in the course of trying to win rewards. The fine wire microelectrodes used to make these measurements cause no discomfort; they are similar to those used in awake humans for the treatment of Parkinson's disease and epilepsy.

In one set of experiments, monkeys learned to reason about probabilities. Imagine predicting the weather based on a set of conflicting and unreliable clues. The monkey's job was to predict which of a red or green target would hold the key to a reward. The clues were a series of shapes, presented one after another on a video monitor, giving only probabilistic evidence for red or green. While a monkey viewed these clues, we found neurons that added and subtracted the evidence towards red or green (examples at http://www.shadlen.org/mike/movies/ProbClass). When the monkey was allowed to choose before the end of the sequence, he made his decision when the accumulated evidence reached a critical level, or threshold. These neural calculations closely resemble mathematics developed by Alan Turing to decide whether a pair of intercepted messages was encrypted on identical Enigma machines. This was determined when the accumulated evidence (from letter alignments) reached a threshold.

Most of the studies I will present are published, but we will report two new findings at SfN2008. One concerns the mechanism underlying confidence in a decision. We are able to ask a monkey how confident he is after a decision by giving him a chance to opt instead for a certain reward. The reward is desirable but less so than the one he would obtain for a correct decision. Such a post-decision wager is thought by some to be a sign of conscious awareness of one's behaviors. We discovered that the decision-making neurons also signal the level of the monkey's confidence in his decision. This experiment and related ones with humans and rats expose the neural code for "degree of belief".

The second unpublished experiment was performed with human subjects. It shows for the first time why, after we make a decision, we occasionally change our mind and make a better decision, even when no additional evidence is provided. Here is the paradox. If we have information to make a better decision, why don’t we use it to make a better decision in the first place? The decision-making mechanism discovered in the monkey resolves this paradox. When the brain terminates a decision based on the accumulated evidence, there is often additional information wending its way through the brain. Our experiment confirms that this is the mechanism by which humans refine their decisions.

These explorations of decision-making build on advances in understanding visual processing and motor function made over the past several decades, mainly through recording and stimulating neurons in the brains of nonhuman primates. However, disorders affecting cognition largely preserve sensory and motor function. What goes awry is the stuff in between: interpretation, recall, concentration, deduction, inference, etc. The study of decision-making offers a window onto these complex processes, paving the way to novel treatments of mental and neurological disorders, and pointing the way toward a neuroscientific understanding of cognition.

Speaker's Summary

Speaker: Geoffrey Schoenbaum, MD PhD **(410) 706-3814**
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Special Lecture: **A New Perspective on the Role of Orbitofrontal Cortex in Decision-Making, Judgment, and Adaptive Behavior**

Monday, November 17, 8:30–9:30 a.m., Washington Convention Center, Hall D

Humans and other animals have the ability to change their behavior when things don't go as expected. A failure to engage this ability is the basis of much that is comic and pathological in human behavior. Be it Homer Simpson, Macbeth, or the politicians in Washington, the humor or pathos of these situations derives from the protagonists' inexplicable inability to learn from their mistakes. Why can't they stop! Modifying one's behavior in response to unexpected outcomes requires at least two things - first you must recognize that an outcome occurred that was not predicted in advance and second you must use that signal to engage learning so that future predictions will be more accurate. Current theories propose that the latter function — the teaching signals — come from a small population of neurons located deep in the brain. I will discuss new evidence suggesting that the former function — the ability to recognize an unexpected outcome at all - depends critically on a completely different area located in the frontal lobes — the orbitofrontal cortex (OFC). This area is well-known for its role in good judgment — allowing us to use what we think we know about likely outcomes to guide decision-making. However it now appears the OFC is also important for allowing us to recognize — and learn — when things don't quite go as expected.

Speaker's Summary

Speaker: Okihide Hikosaka, MD PhD **(301) 402-7959**
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Role of the Primate Lateral Habenula in Negative Motivational Control of Oculomotor Behavior

(698.5)
Symposium: Habenula: Crossroad Between the Basal Ganglia and the Limbic System
Wednesday, November 19, 10:20–10:55 a.m., Washington Convention Center, Ballroom B

In the human brain the cerebral cortex is so dominant that it is virtually the only structure visible from outside. Hidden below the magnificent cerebral cortex, however, are many smaller structures. The habenula is one of such small subcortical structures.

Masayuki Matsumoto and I stumbled into this structure while we were recording the electric activity of neurons in the brain of a rhesus monkey. On this day we were offering sweet raisins to the monkey as usual. We then decided to be slightly mischievous. Now, instead of opening our hand to reveal a raisin, we opened our hand and there was nothing. Gazing at the empty hand, the monkey raised his eyebrows and showed his teeth, disgruntled to be denied his tasty treat. At the same time many neurons in the habenula emitted a burst of activity in unison as if it had been the expression of anger or disappointment. This discovery hinted at the nature of the habenula, but it needed to be tested more rigorously, and for that we used computer games.

Our monkeys are hardcore gamers, and they do the games to get rewards. Each time the monkey wins the game, he gets a small amount of juice as a reward. The game starts with a spot of light (target) on the center of the screen, which then jumps to the right or left. The monkey wins the game if he can continue to look at the target and follow it quickly as it jumps to one side. Most importantly, the amount of reward is different depending on which direction the target has jumped (e.g., left-large, right-small), and this directional bias of reward is reversed occasionally to the monkey's surprise. We found that a majority of neurons in the habenula were excited if the target direction told the monkey that a large reward was coming, but then a small reward was given instead - much as they had been excited by our 'empty hand' procedure described above. In contrast, the neurons were inhibited when a large reward was given unexpectedly. In other words, the activity of habenula neurons reflected the difference between the actual amount of the reward and the predicted amount of the reward. This value is called the 'reward prediction error'.

The signal related to reward prediction error has been considered vital in learning how to get as much reward as possible. To put it simply, this signal tells how you should change your behavior until you have reached your ideal goal. It has been shown that a group of neurons called dopamine neurons which are located in the basal ganglia (one of the largest subcortical structures) carry signals related to positive reward prediction errors. If you lose your dopamine neurons, you would become unable to move your body voluntarily, as commonly seen in Parkinson's disease. It might sound strange that the loss of reward-information-carrying neurons leads to the loss of voluntary movement, but this indicates how deeply reward-related motivation is related to motor behavior.

An important but insoluble question has been how dopamine neurons acquire such sophisticated information as the reward prediction error signal. Our discovery raised the possibility that the habenula could be a major source of the reward prediction error information that is expressed in dopamine neurons. To test this possibility we artificially activated habenula neurons with a very small electric current. We found that almost all dopamine neurons we recorded stopped their activity immediately after the habenular stimulation. This means that reward prediction error signals are transmitted from the habenula to dopamine neurons. Interestingly, increasing activity in the habenular neurons reduces activity in the dopamine neurons, which means that they must be connected through an inhibitory neuron.

Habenula neurons and dopamine neurons appear to have a Reward & Punishment relationship. Dopamine neurons may represent something pleasurable, whereas habenula neurons may represent something harmful. In fact, excessive dopamine in the brain is known to lead to excessive excitement. What about excessive activity in the habenula? Some previous studies have indicated that excessive habenular activation is correlated with depressive mood and behaviors. Furthermore, there have been suggestions that psychiatric disorders, including depression and schizophrenia, are caused by abnormal activity of habenular neurons. Recent papers even proposed deep brain stimulation targeting the habenula as a therapy for depression. Someday, patients with drug-resistant depression may be able to stimulate their own habenula, causing their persistent harmful thoughts and depressive moods to disappear, thus allowing them to achieve their goals.

Speaker's Summary

Speaker: Patricia Churchland, BPhil **(858) 534-6811**
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David Kopf Lecture on Neuroethics: **How Do Brains Navigate Their Social/Moral Worlds?**
Monday, November 17, 10–11 a.m., Washington Convention Center, Hall D

What can neuroscience teach us about morality?

Recent developments in the neuroscience of social bonding in mammals suggest that moral behavior — and social behavior more generally — is anchored by social attachment and trust. This perspective on sociality contrasts with a longstanding tradition in moral philosophy according to which human moral behavior is unrelated to social behavior in nonhuman animals. According to that approach, morality derives from a uniquely human capacity to reason, or possibly from a supernatural relationship to a divine being.

Social animals, such as humans, have a powerful urge to be with those to whom they have become attached. We feel safe in their company and anxious when separated. These effects appear to be regulated by simple neurochemicals, oxytocin and vasopressin. Oxytocin-release is a safety signal, and reduces fear responses while allowing for the emergence of affiliative behavior such as grooming and 'friendliness'. In some social mammals, such as prairie voles and marmosets, the release of oxytocin and vasopressin during the first mating sets the stage for life-long pair bonding. Oxytocin released during birth and suckling also plays a role in the bonding of mother and offspring. Human infants deprived of normal cuddling have more difficulty forming stable bonds later in life.

Attachments *per se* do not specify exactly what action should be performed in what condition. They are best conceived as dispositions that contour social-problem space. Come the time to act, trust and attachment may be expressed in behavior as the outcome of a problem-solving process in neural networks known as *constraint satisfaction*. Though not understood in detail, this process involves constraints that include emotions, evidence, habits, expectations of others, cultural practices, and predictions concerning consequences. Relative to context, these dispositions might be expressed by grooming a consort, attacking intruders, or nurturing a baby.

The hypothesis fits with an ancient, but currently unfashionable tradition, originating with Aristotle's observations about the importance of social skills rather than absolute rules, and his theories concerning the incremental improvement over time of cultural practices.