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VIRTUAL REALITY HELPS RESEARCHERS TRACK HOW BRAIN RESPONDS TO SURROUNDINGS

Video game-based technologies allow new insight into memory, perception, and motor control

SAN DIEGO — New tools inspired by video games are revealing how the brain senses and responds to its surroundings, finds new human and animal research. Taking advantage of state-of-the art technologies to track and mimic real-life environments, these studies show with new detail how the brain navigates, identifies, and remembers a setting. In additional human research, scientists apply these same technological advances to help people who have experienced strokes regain skills.

The results were presented at Neuroscience 2010, the annual meeting of the Society for Neuroscience and the world's largest source of emerging news on brain science and health.

Today's new findings show that:

- Activity in rats' memory-related brain areas varies with how quickly they move to explore their environments. An optogenetics study suggests that the speed with which an animal — or a person — moves in a setting could alter memories of that setting (Loren Frank, PhD, abstract 100.8, see attached summary).
- Older rats appear unable to distinguish similar objects — behavior comparable to that of elderly people, who often have memory and perception troubles. Researchers suggest the rats' actions may be similar to those of young rats with damage in specific brain regions (Sara Burke, PhD, abstract 204.5, see attached summary).
- Repeated exercise in a virtual environment helps stroke patients improve arm and hand function, according to a new human study of an interactive video game-based therapy (Sergei Adamovich, PhD, abstract 84.12, see attached summary).

Other research findings being discussed at the meeting show:

- Studying mice walking in a virtual reality environment enabled researchers to capture brain activity patterns with single nerve cell resolution, more than 100 times more precise than common imaging techniques. The new method allows for new types of experiments on the "place cells" that create the brain's representation of location and space (David Tank, PhD, see attached speaker's summary).

"Our brains continuously change as we experience the world," said Veronique Bohbot, PhD, of the Douglas Mental Health University Institute and McGill University, the press conference moderator and an expert in auditory and visual spatial memory, virtual reality, and brain plasticity. "New technologies and research methods now allow researchers to study that change, investigating individual differences in the way people use spatial memory, navigation, and motor function, as well as implications for the use of navigation devices such as GPS. Many potential real-life therapies inspired by video games are already emerging from the virtual world."

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

– more –

Related Presentation:

Symposium Session 213: **Removing Brakes on Adult Brain Plasticity: Molecular, Cellular, and Behavioral Interventions**
Sunday, Nov. 14, 2010, 1:30–4 p.m. PST, Room 6B
# # #

Abstract 100.8 Summary

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Brain Cell Communication in Memory Center Varies with Animals' Movements

Optogenetics study suggests motion determines how an experience is stored in memory

Activity in rats' memory-related brain areas varies with how quickly they move to explore their environments, according to a new study. The research was presented at Neuroscience 2010, the annual meeting of the Society for Neuroscience and the world's largest source of emerging news about brain science and health. The result suggests that the speed with which an animal — or a person — moves in a setting alters the memories of that setting.

"Our behavior seems to influence what we remember," said senior author Loren Frank, PhD, at the University of California, San Francisco. "We are encouraged to 'stop and smell the roses' with the idea that slowing down to take in our surroundings will enhance our memories of those experiences. But we don't know if the way we move changes the way we learn."

Rats placed in an unfamiliar room will move slowly and explore, even if food is present, while rats put in a familiar space rush to find food. While these behaviors are well-documented, how brain circuits change with different patterns of motion and exploration is unknown. The hippocampus, a brain circuit essential for memory formation, was thought to process memories in two ways: recording memories during movement and consolidating memories during immobility. But the new study shows that memory circuits change continuously.

The authors used optogenetics to make neurons in the hippocampus sensitive to light. When the neurons were laser-activated, the researchers could measure the flow of activity through the circuit as animals learned about a new place. They found that the pathway associated with storing and consolidating memories was most active when the animals moved slowly. At faster speeds, the balance shifted from these circuits to circuits bringing in info from the outside world.

"Our results suggest that the way an animal explores its environment could have a profound effect on how the memories for that experience are stored," Frank said.

Research was supported by Alfred P. Sloan Foundation, the Swartz Foundation, the John Merck Fund, the Helen Hay Whitney Foundation, the National Science Foundation, and the National Institutes of Health.

Scientific Presentation: Saturday, Nov. 13, 4–5 p.m., Halls B–H

100.8, Encoding to consolidation: An optogenetic probe reveals continuous modulation of hippocampal information processing by behavioral state
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TECHNICAL ABSTRACT: Neural processing in the hippocampus is crucial for memory encoding, retrieval, and consolidation. In current models there are two distinct states of hippocampal processing, one devoted to encoding and one devoted to retrieval and consolidation. These two states have been linked to two states of animal behavior, locomotion and stillness/slow wave sleep. This two state model has been very influential, but are there really two distinct states? Here we used a combination of optogenetic manipulation, electrical stimulation, and recording in behaving rats to show that behavioral state continuously modulates information processing in the hippocampal circuit. We first used a lentivirus with a CamKIIα to express channelrhodopsin-2 selectively in rat dentate gyrus granule cells and their mossy fiber projections to CA3. We developed a combined fiber optic / multielectrode microdrive array, allowing us to optically activate the mossy fiber pathway while recording activity in both CA3 and CA1. Examining field responses to optical activation, we found that the modulation of information processing by behavior is not a switching between moving and still states, but rather a continuum. Specifically, the strength of the signal in CA1 as measured by the slope of the field EPSP was large when animals were still and decreased by a factor of as much as three as animals moved at progressively faster speeds. This effect was also seen when we used electrical stimulation to activate the CA3 Schaeffer collateral inputs to CA1, indicating that it could be explained by modulation of the CA3 - CA1 pathway. Moreover, log(movement speed) could account for up to 60 percent of the variance in EPSP slope for both optical and electrical stimulation experiments. This result yields specific predictions about how movement should control the flow of information activity through the hippocampal circuit, all of which were verified by separate analyses (see abstract from M. F. Carr). Thus, our results indicate that a two state model is inadequate for understanding hippocampal information processing. Instead, our findings point to a dynamic balance of pathway strength - regulated by speed - that determines the outputs of the hippocampal circuit.

Abstract 204.5 Summary

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Older Animals Unable to Distinguish Similar-Looking Objects

Study suggests old rats had same trouble recognizing items as brain-damaged young rats

Older rats appeared unable to discriminate between objects with similar features, behavior comparable to that of elderly people, who often have memory and perception troubles. The older rats' actions may be similar to those of young rats with damage in specific brain regions, according to a new study. These results were presented at Neuroscience 2010, the annual meeting of the Society for Neuroscience and the world's largest source of emerging news about brain science and health.

"A symptom of aging is a decreased ability to distinguish something novel from something familiar," said study author Sara Burke, PhD, of the University of Arizona. "Our experiment implies that this might be caused by age-related changes in the perirhinal cortex, an area of the temporal lobe associated with both memory and perception."

As rats age, they display some of the same cognitive impairments that humans do. Young rats are quick to discern new objects, exploring unfamiliar things for several seconds more than items they have previously encountered. But while old rats can classify unfamiliar and familiar items over the short term, they become confused as time passes, and eventually act as though unknown objects are well-known. In this study, researchers explored how older rats would react to known objects that are similar but distinct in appearance.

Burke and her team compared the behavior of old rats with young. Each rat was first given two identical objects and was then presented with either an identical object, or an object similar but distinctly different from the previous ones. Only the young rats extensively explored the novel object. The older rats explored the alike and unalike objects for the same amount of time, indicating they were unable to tell them apart.

"Because their behavior was reminiscent of rats with perirhinal cortical lesions, it is possible that this behavioral deficit is caused by age-related changes targeted that area of the brain," Burke said. "Such alterations could contribute to the increased incidence of false memories experienced by elderly individuals."

Research was supported by the National Institute on Aging, the McKnight Brain Research Foundation, and the Arizona Undergraduate Biology Research Program.

Scientific Presentation: Sunday, Nov. 14, 8–9 a.m., Halls B–H

204.5, The effect of perceptual difficulty and age on spontaneous object recognition
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TECHNICAL ABSTRACT: Normal aging causes a decline in object recognition (e.g., Burke et al., 2008) but the extent to which this deficit arises from memory or perceptual impairments is a matter of debate. Importantly, lesions of the perirhinal cortex also lead to impaired object recognition (Winters & Bussey, 2005), and these deficits can be observed under conditions with no memory load (a zero second delay) when the two distinct test objects share common features (Bartko et al., 2007). This observation supports the idea that the perirhinal cortex performs both perceptual and mnemonic functions (e.g., Murray & Bussey, 1999). The current experiment investigated the ability of young and aged rats to distinguish between two different objects that shared common features. Young and old rats performed a variant of the spontaneous object recognition task in which there was a minimal delay (<30 sec) between the sample and the test phase. In one condition the familiar object shared no common features with the novel object (low perceptual difficulty). In the other condition the familiar object and the novel object contained overlapping features (e.g., both objects were similar in size and shape; high perceptual difficulty). During the test phases of both conditions, the young rats showed a significant exploratory preference for the novel relative to the familiar objects, although the novelty preference was attenuated for the high relative to the low perceptual difficulty condition. In contrast, the aged rats only showed a significant exploratory preference for novel compared to familiar objects during the low perceptual difficulty condition. When the familiar and novel objects shared common features the aged rats did not distinguish between the two objects, as revealed by their exploratory behavior. Because the data obtained from the old rats are reminiscent of observations from rats with perirhinal lesions (Bartko et al., 2007), the current findings suggest that aged rats have difficulty resolving perceptual ambiguity. This may arise from functional changes within the perirhinal cortex that occur over the lifespan.

Abstract 84.12 Summary

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Video Game-Based Therapy Helps Stroke Patients Recover

Study finds patients who practice in a virtual environment improve arm movement

Repeated exercise, even in a virtual environment, helped stroke patients improve arm and hand function, according to a new human study of an interactive video game-based therapy. The findings were presented at Neuroscience 2010, the annual meeting of the Society for Neuroscience and the world's largest source of emerging news about brain science and health.

"We are using an innovative approach to rehabilitation," said study author Sergei V. Adamovich, PhD, of the New Jersey Institute of Technology. "In virtual environments, individuals with arm and hand impairment practiced tasks such as reaching and touching virtual objects. They took a cup from a shelf and put it on a table, hammered a nail, and even played a virtual piano."

Even years after a stroke occurs, people with disabled limbs still sometimes show improvement with therapy. Though recent studies have shown recovery is possible, researchers aim to further increase the amount of improvement in the speed and fluidity of motor control. In this study, 24 participants who had a stroke at least six months prior to therapy practiced with the video game for about 22 hours over a two-week period. With the aid of a robotic arm, individuals attempted increasingly difficult tasks. Adamovich and his colleagues observed that the volunteers moved their hands faster over the course of the tests.

The researchers also examined whether therapy changed the participants' brains to improve motor functions. In ongoing trials, the authors use transcranial magnetic stimulation and functional magnetic resonance imaging to map connections in the volunteers' brains as they undergo rehabilitation.

"Our preliminary data suggest that, indeed, robot-assisted training in virtual reality may be beneficial for functional recovery after chronic stroke," Adamovich said. "Furthermore, our data imply that this recovery may be particularly due to increased functional connections between different brain regions."

Research was supported by the National Institute of Child Health and Human Development and by the National Institute on Disability and Rehabilitation Research.

Scientific Presentation: Saturday, Nov. 13, 4–5 p.m., Halls B–H

84.12, Strengthened functional connectivity in bilateral sensorimotor cortex of chronic stroke patients after robot-assisted training in virtual reality: A pilot study
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TECHNICAL ABSTRACT: We investigated functional reorganization of brain activity in two chronic stroke subjects after intensive training of their affected upper extremity using adaptive robot-assisted virtual reality therapy. Subjects trained three hours/day for eight days on gaming simulations in interactive virtual environments. Motor tasks involved reaching for stationary and moving targets in 3D space or flexing/extending the arm and fingers. Clinical outcome measures included the Jebsen Test of Hand Function (JTHFT) and Wolf Motor Function Test (WMFT). Neurophysiological outcomes included functional MRI (n=2), and motor evoked potentials (MEP, n=1). Outcomes were acquired two weeks before, one to two days before, and one to two days after the intervention. During the fMRI sessions subjects performed a finger flexion task with their affected hand toward a set of target angles. To ensure subjects maintained consistent movements in the scanner across sessions, we provided subjects with real-time visual feedback of their movement by streaming data from an MRI-compatible data glove to animate VR hand models displayed on a screen. fMRI data was preprocessed and analyzed in SPM5. For MEP measurements, neuronavigated single-pulse TMS was applied to the region in the lesioned and non-lesioned hemisphere eliciting the strongest response in the contralateral FDI muscle. Subjects demonstrated improvements in WMFT time (10 percent and three percent) and in JTHT time (10 percent and six percent). fMRI data showed that movement (versus rest) was associated with extensive activation in a bilateral sensorimotor network involving cortical and subcortical regions. The magnitude and extent of activation in frontal and parietal sensorimotor areas was markedly reduced after training. In a secondary analysis, we tested the hypothesis that training may have invoked strengthened functional connectivity (correlation) among regions. For this, we performed a voxel-wise correlation between each voxel in the brain and the mean activity in a 10 mm region of motor cortex in the lesioned hemisphere. Both subjects demonstrated significantly increased functional connectivity among bilateral sensorimotor and premotor regions after training. In one subject, we also measured TMS-induced MEPs in each hemisphere. After training, MEP amplitude increased (22 percent) in the lesioned hemisphere but decreased (26 percent) in the contralesional hemisphere. These pilot data suggest that training in our VR simulations may be beneficial for functional recovery after chronic stroke. Further, our data suggest that functional recovery may be attributed to increased functional connectivity among distributed neural regions.

Speaker's Summary

Speaker: David Tank, PhD (609) 258-7371
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Functional imaging of hippocampal place cells at cellular resolution during virtual navigation (203.18)
Poster Session: Learning and Memory: Gamma and Theta Activity
Sunday, Nov. 14, 9–10 p.m., San Diego Convention Center, Halls B–H

We have developed methods to image neuronal activity with sub-cellular resolution in the brains of mice that are navigating in a virtual reality environment. We used our methods to study the fundamental question of whether an anatomically organized map of an animal's local environment exists within a brain structure known as the hippocampus.

Spatial navigation is a widely employed behavior in rodent studies of the neuronal circuits underlying cognition, learning and memory. The neuronal activity underlying mammalian navigation represents one of the most striking examples of behavioral correlation in the brain. Neurons known as place cells found in the hippocampus, for example, are active only in specific locations (place fields) of a local environment. These neurons are part of the navigation circuitry that mammals use to find their way to specific destinations. It has previously been postulated that the place cells within the hippocampus may be anatomically organized into a map of the local environment in which the location of a place cell's place field in the environment is related to the place cell's physical location within the hippocampus. Until now, nearly all recordings from neurons in the navigation circuitry have been performed with extracellular electrodes (small wires placed into the brain), which are not able to directly measure the spatial organization of place cells. Moreover, using electrode methods, it has been difficult to dissect out the circuitry responsible for the firing properties of place cells.

To address these limitations and open new research directions for studying the circuitry underlying mammalian behavior, we have developed methods to image the activity of hippocampal place cells with sub-cellular resolution in mice navigating along a track in a virtual reality environment. Specifically, we used two-photon microscopy, a laser scanning microscopy method, to image with micron-scale resolution in the intact brain. Because the place cells in the hippocampus are located deeper than conventional two-photon microscopy can image, we developed a hippocampal window that allowed us to directly image the place cells. In order to optically record the activity of the neurons using our microscopy methods, we induced the neurons to express a genetically encoded calcium sensitive protein (a protein that changes its fluorescence properties depending on the activity of the neurons). Sub-cellular resolution imaging requires a great degree of mechanical stability; this was achieved by having the mice walk on the surface of an air supported ball, known as a spherical treadmill, while their head remained stationary. Finally, in order to study navigation behaviors we used a visual virtual reality system to display a virtual world around the mouse. The position and view of the virtual environment was updated based on the running speed and direction of the mouse on the spherical treadmill.

Using our methods, we were able to image the activity of about 100 neurons in the hippocampus during virtual navigation. We identified place cells based on their activity patterns and, because of our imaging based approach, we were able to directly identify the physical location of the place cells with respect to each other. We found that if two cells are separated by more than a few cell diameters, no strong relationship exists between the distance between place cells in the physical space of the hippocampus and the distance between their place fields in the virtual environment (i.e. we found no evidence for an anatomically organized map on the local scale within the hippocampus). The combination of virtual reality, high-resolution functional imaging and genetic tools should allow for a new generation of studies to probe neuronal circuit dynamics during behavior.