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Early Sensory Experiences Shape Brain Structure and Function

Animal research shows that too much or too little sensory stimulation can affect how the brain develops

SAN DIEGO — Environmental enrichment, sensory stimulation, and sensory deprivation all shape the connections and organization in the brain, in addition to affecting behavior, as shown by new research presented at Neuroscience 2016, the annual meeting of the Society for Neuroscience and the world's largest source of emerging news about brain science and health.

The brains of animals, including humans, adapt throughout the course of their lifetimes. Every experience changes the brain in some way, but sensory experiences in particular profoundly influence brain development. And those that occur very early in development carry the most impact on brain structure and function.

Today's new findings show that:

- Rats raised in a natural, outdoor environment show differences in brain organization and behavior from rats raised in standard laboratory cages (Leah Krubitzer, abstract 807.12, see attached summary).
- Mice exposed to excessive sensory stimulation early in life are more impulsive and susceptible to cocaine (Jan-Marino Ramirez, abstract 392.10, see attached summary).

Other recent findings discussed show that:

- The auditory brain structure of a person deaf from birth appears the same as that of a hearing person (Ella Striem-Amit, abstract 48.09, see attached summary).

"Today's findings show the progress we're making in understanding how early sensory experiences affect brain development and future behavior," said press conference moderator Gina Turrigiano, PhD, of Brandeis University. "A better understanding of how early experiences shape the brain will help us prevent and treat neuropsychiatric illnesses and other brain disorders."

The research was supported by national funding agencies such as the National Institutes of Health, as well as other public, private, and philanthropic organizations worldwide. Find out more about sensory development at *BrainFacts.org*.

Related Neuroscience 2016 Presentation

Presidential Special Lecutre: Tuning Auditory Circuits for Vocal Communication
Saturday, Nov. 12, 5:15 p.m.-6:25 p.m., SDCC Ballroom 20

Abstract 807.12 Summary

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Growing Up in a Natural Environment Changes the Brains and Behavior of Rats
Rats raised outdoors differed from those raised in standard laboratory conditions

Raising rats in a natural environment alters their brain wiring and affects how they behave, according to new research released today at Neuroscience 2016, the annual meeting of the Society for Neuroscience and the world's largest source of emerging news about brain science and health.

Brains undergo changes throughout an animal's life, but experiences that take place early in life, when the brain grows and develops very rapidly, have the largest impact on the brain's structure and connections. The organization of the brain in turn shapes how humans and other animals move, perceive the world, and behave.

In this study, researchers investigate how environment shapes the brain by comparing rats raised in standard laboratory cages with rats raised in an outdoor, seminatural environment roughly 3,000 times the size of a rat cage. Being outdoors exposed the rats to many things absent in a laboratory, such as changing weather conditions and the sights, smells, and sounds of wild animals, including predators. The large outdoor cage had a dirt floor containing wild plants and invertebrates, allowing the rats to burrow and hunt insects, as well as mesh walls and branches they could climb. These behaviors, typical of wild rats, require skills that laboratory-housed rats cannot practice.

Rats reared outdoors developed more slowly in some ways, opening their eyes a day later and learning to roll over later. However, the outdoor rat pups (particularly the female pups) learned to walk faster than laboratory-raised rat pups. In adulthood, the brains of outdoor-raised rats differed from lab-raised rats: The area of the brain controlling voluntary movements devoted a larger region to trunk, tail, and hindlimbs, all of which are used extensively in climbing.

"While we recognize that genes can contribute to individual variability among humans and other mammals, our experiments address the puzzle of how individual differences emerge as a result of the environment in which they are reared," said lead author Leah Krubitzer, PhD, of the University of California, Davis. "We cannot yet say which factors lead to the many differences we observed, but this study is a useful first step in understanding how different environments shape developing brains and the behavior that brains ultimately produce."

Research was supported with discretionary funds from UC Davis.

Scientific Presentation: Wednesday, Nov. 16, 4-5 p.m., Halls B-H

17385. Rats gone wild: How seminatural rearing of laboratory animals shapes behavioral development and alters somatosensory and motor cortex organization
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TECHNICAL ABSTRACT: The mammalian neocortex and the behavior it generates are highly adaptable. Few species exemplify this better than rats, which for thousands of years have thrived everywhere that humans have settled; traveling in our ships, living in our houses and cities, and eating our food despite an unending campaign of cats, traps, and poisons. Such adaptability to various climates, habitats, food sources, and predators is due, in part, to well-established sensitivity of the mammalian cortex to environmental conditions during development. This early experience can shape sensory and motor cortical maps, leading to behavior adapted to the local environment. Most studies of this process are necessarily restricted to laboratory animal models reared in a relatively deprived environment. Here we take a different approach and investigate how early natural environmental experiences shape neocortical development. We compare control rats reared in standard laboratory cages with genetically identical rats reared in an outdoor, seminatural environment: large wire mesh enclosures (9.75 X 2.5 X 2.5 m) roughly 3000 times the size of a standard rat cage. These field pens, located in a nature reserve, expose rats to weather (e.g. 12.8-43.3 °C, 4-100% humidity), day/night length and sun/moon light level conditions, as well as the sights, sounds, and smells of wild animals, including predators. A dirt floor populated by wild plants and invertebrates permits burrowing and hunting, while the mesh walls and introduced branches promote climbing. These are atavistic behaviors typical of wild rats and require sensorimotor processing entirely absent in standard laboratory cages. 24-h video recordings were made with overhead infrared cameras in the enclosure and the burrow box from which social behaviors were scored across the lifetime. Electrophysiological sensory mapping and intracorticalmicrostimulation in adult anesthetized animals were used to examine the organization of somatosensory and motor cortex. Our preliminary data indicate that seminatural rearing shifts the timing of neurobehavioral development as well as adult exploratory, social, and cognitive behaviors. These behavioral alterations are associated with changes in the representation of movements in motor cortex, with relatively more cortical area devoted to the representation of trunk and tail movements at the expense of neighboring movement domains. Such data are critical for understanding how distinct phenotypes emerge from a single genotype based on differential early experience.

Abstract 392.10 Summary

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Exposure to Excessive Sensory Stimulation Leads to ADHD-Like Behaviors in Mice
Increased audio and visual stimulation early in life changed animals' brains and behvaior

Excessive sensory stimulation early in life may cause behaviors reminiscent of attention deficit hyperactivity disorder (ADHD) in mice, according to new research released today at Neuroscience 2016, the annual meeting of the Society for Neuroscience and the world's largest source of emerging news about brain science and health.

Observational studies in humans link excessive use of fast-paced media during early childhood to attentional deficits. Researchers posit that excessive sensory stimulation could affect susceptibility to developing disorders like ADHD. Using a mouse model, researchers explored how increased sensory stimulation might alter brain function and behavior and infleunce the risk of developing neuropsychiatric disorders.

The team studied mice exposed to audio-visual stimulation for six hours a day for several weeks starting when they were 10 days old. After the exposure period, the mice displayed pronounced hyperactivity behaviors, impaired learning and memory, and increased risk-taking behavior.

In humans, ADHD is often associated with substance abuse, and in the mouse model, researchers found that mice exposed to excessive sensory stimulation were more susceptible to cocaine, and their brains showed changes in specific addiction-related areas.

"Our research indicates that excessive exposure to sensory stimulation in early life has significant effects on behavior and brain circuits in mice," said senior author Jan-Marino Ramirez, PhD, of Seattle Children's Research Institute. "This study has important implications in today's increasingly complex technological age, where children face a tremendous amount of sensory stimulation. Our rodent model could be used to gain a better understanding of the potential effects of extensive audio-visual media use in young children."

Research was supported with funds from the Seattle Children's Research Institute.

Scientific Presentation: Monday, Nov. 14, 2-3 p.m., Halls B-H

17383. Consequences of excessive sensory stimulation during development on addiction, impulsivity, and attention
*S. RAVINDER, S. GADIWALLA, D. CHRISTAKIS, S. FERGUSON, **J.-M. RAMIREZ**;
Seattle Children's Res. Inst., Seattle, WA

TECHNICAL ABSTRACT: Early life experiences exert long-lasting effects on neural function, which can have a deep impact on behavior and vulnerability to developing neuropsychiatric illnesses such as Attention deficit hyperactivity disorder (ADHD). Most ADHD research has focused on understanding genetic causes, but there remains a large role for environmental factors in the etiology of this disease. We have developed a rodent model of "excessive sensory stimulation (ESS)" whereby mice are exposed to audio-visual stimuli for 6 h/day, from P10-P52 (Christakis et al., Sci Rep., 2012). When subsequently tested, ESS mice demonstrate numerous behavioral outcomes that are reminiscent of the clinical symptoms of ADHD (inattentiveness, impulsivity, hyperactivity). Compared to controls, ESS mice show poorer short-term memory, impaired learning and attention in memory tests; hyperactivity and increased risk-taking in multiple anxiety tests. ADHD is known to be highly comorbid with substance abuse. Here we investigated the relationship between ESS and vulnerability to drugs of abuse in adulthood. We found that ESS mice displayed locomotor hyperactivity that develops over time but showed blunted psychomotor sensitization to cocaine when compared to controls. Interestingly, ESS mice develop a stronger conditioned place preference for cocaine compared to controls, suggesting that they may have a higher addiction liability. To further characterize the behavioral impact of ESS, we are currently examining the effects of ESS in the 5-choice serial reaction time test and the delay-discounting test, both of which are well-established models for testing impulsivity and attention. Our initial data from the delay discounting test suggests that ESS mice make more impulsive choices than controls. At the cellular level, our experiments show that ESS leads to an increase in miniature excitatory postsynaptic currents in the nucleus accumbens, amygdala and medial prefrontal cortex (mPFC). We are currently pursuing experiments to further characterize these cellular effects. Many studies have shown that changes in the frontal cortex may underlie impulsivity and attention in animal models and ADHD symptoms in humans. In future experiments, we plan to modulate *in-vivo* activity in the mPFC of ESS and control mice to explore the role of this brain region in ESS induced changes in impulsivity and attention. Our study has important implications in today's increasingly complex technological age where children face a tremendous amount of sensory stimulation that could interact with genetic predispositions to produce detrimental effects on behavior and brain function.

Speaker Summary 48.09

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The Deaf Person's Auditory Brain Architecture Is Identical to That of a Hearing Person
Saturday, Nov. 12, 1-2 p.m., Halls B-H

Does our brain need for us to hear or see in order to develop properly? What happens in people who are born profoundly deaf? It is widely known that infants born with significant hearing impairment must undergo cochlear implantation very early in life. If they do not, auditory deprivation during sensitive periods in early development would affect their brain development, and their hearing would not develop properly. However, it is not clear what are the causes of this loss of function.

This study shows the deficit does not result from the way in which the brain organizes its auditory sense architecture, which remains intact even in people who are deaf from birth, even though parts of these regions respond to sight. The new findings show that the underlying connectivity of the auditory cortex, which links together regions according to their preferred sound frequency, can develop on its own without any actual auditory experience.

The study was conducted by placing hearing volunteers in an MRI scanner and tracking which areas in the auditory cortex were activated by different tones. Then, hearing and deaf subjects were asked to lie down quietly in the scanner, while their brain activity was tracked over several minutes. This allows us to map which areas are functionally connected (show similar, correlated patterns of activation) to each other. We then used the areas showing tone-preference in the "tonotopic" map to study the functional connectivity profiles in the hearing and congenitally deaf groups. We found that the network profiles related to tone preference in adults born deaf was indistinguishable from that discovered in hearing people, all the way to the auditory language-processing regions.

Interestingly, this auditory-like organization was found even though parts of the auditory cortex of deaf adults may have plastically changed to respond to visual information. In a previous study conducted by some team members on the same participants, it was possible to "read out" (decode) information about the location of visual patterns from the auditory cortex of the deaf. Still, the new findings show there is a balance between change and typical organization, such that even when the auditory cortex shows plasticity to processing vision, its typical auditory organization can still be found.

The new findings in the deaf corroborate recent discoveries showing intact spatial topographical maps in the visual cortex in people born blind. Together, these findings stress the importance of prenatal and innate factors in brain development, dispelling the nearly half-century belief that the sensory brain regions crucially depend on sensory experience early in life to develop properly.

What does that mean for millions of deaf and blind people living today? These findings join scientific advances in developing sensory prostheses, sensory substitution devices, stem cell transplantations and multisensory rehabilitation techniques, which will hopefully be able to rehabilitate the senses even in adults suffering from blindness or deafness.

Research was supported with funds from the National Basic Research Program of China, the National Natural Science Foundation of China, the European Union's Horizon 2020 Research and Innovation Programme under a Marie Sklodowska-Curie grant, the Israel National Postdoctoral Award Program for Advancing Women in Science, and a Fundação BIAL grant.