Embargoed until Oct. 14, 3:30 p.m. CST
Press Room, Oct. 13–17: (504) 670-4630

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DEVELOPING BRAIN IS SOURCE OF STABILITY AND INSTABILITY IN ADOLESCENCE

New findings on depression, decision-making, and cognition in the teen brain

NEW ORLEANS — Scientists presented new research today on how the brain develops during the dynamic and vulnerable transition period from childhood to adulthood. The findings underscore the uniqueness of adolescence, revealing factors that may influence depression, decision-making, learning, and social relationships. The findings were presented at Neuroscience 2012, the annual meeting of the Society for Neuroscience and the world's largest source of emerging news about brain science and health.

The brain's "reward system," those brain circuits and structures that mediate the experience and pursuit of pleasure, figured prominently in several studies. The studies shed light on adolescents' ability to control impulsivity and think through problems; reveal physical changes in the "social brain;" document connections between early home life and brain function in adolescence; and examine the impact of diet on depressive-like behavior in rodents.

Today's new findings show that:

- Adolescents can throw impulsivity out the window when big rewards are at stake. The bigger the reward, the more thoughtful they can be, calling on important brain regions to gather and weigh evidence, and make decisions that maximize gains (BJ Casey, PhD, abstract 128.04, see attached summary).
- Rodents that receive an omega-3 fatty acid in their diets, from gestation through their early development, appear less vulnerable to depressive-like behaviors during adolescence (Christopher Butt, PhD, abstract 522.07, see attached summary).
- Depression in older adolescent boys may be associated with changes in communication between regions of the brain that process reward. At the same time, the study found possible connections between early emotional attachments — particularly with mothers — and later reward system function (Erika Forbes, PhD, abstract 128.11, see attached summary).
- Early cognitive stimulation appears to predict the thickness of parts of the human cortex in adolescence, and experiences at age four appear to have a greater impact than those at age eight (Martha Farah, PhD, abstract 908.02, see attached summary).
- During the span of adolescence, the volume of the "social brain" — those areas that deal with understanding other people — changes substantially, with notable gender differences (Kathryn Mills, BA, abstract 128.02, see attached summary).

"Advances in neuroscience continue to delve deeper and deeper into the unique and dynamically changing biology of the adolescent brain," said press conference moderator Jay Giedd, MD, of the National Institute of Mental Health, an expert on childhood and adolescent brain development. "The insights are beginning to elucidate the mechanisms that make the teen years a time of particular vulnerabilities but also a time of great opportunity."

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

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Abstract 128.04 Summary

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Driven by Reward, Adolescents Can Harness Impulsivity

Teens take more time than adults to ponder their decisions when big rewards are at stake

While adolescents may be known more for their impulsivity than sound decision-making, new findings show that they take more time than adults to gather and weigh the facts when rewards are at stake. And the bigger the reward, the more time they take. This shows that incentives can be used to help adolescents overcome their impulsivity and harness their brain power, according to the findings presented at Neuroscience 2012, the annual meeting of the Society for Neuroscience and the world's largest source of emerging news about brain science and health.

The brain's reward system mediates the pursuit of pleasure. While it evolved to reinforce behaviors needed for species survival — like eating and sex — it can be activated by a range of activities from drugs to drag racing. In adolescents, this reward system is easily activated, fueling a tendency to act on impulse. But the pursuit of rewards can also help adolescents engage in higher-level thinking, according to new work in a study by senior author BJ Casey, PhD, at Weil Cornell Medical College.

To understand relationships between age and reward sensitivity, the researchers asked adolescents and adults to observe a cloud of randomly moving dots and select the direction in which they were moving. Correct responses came with either a small or large reward. Brain images collected using functional magnetic resonance imaging (fMRI) during the task enabled researchers to correlate behavior with function in different brain regions.

This research showed that in adolescents — but not in adults — the prospect of larger rewards ramped up activity in key regions of the brain's reward system. Adolescents also took longer to make a decision when larger rewards were at stake, a time increase that corresponded with greater recruitment of brain regions thought to be involved in the accumulation and weighing of evidence.

"The three leading causes of death in teens in the United States — accidental death, suicide, and homicide — are preventable," Casey said. "Clearly, some terrible decisions are being made. But our research shows that adolescents can and will control their impulses and think through problems when rewards are at stake."

Research was supported with funds from the National Institutes of Health.

Scientific Presentation: Sunday, Oct. 14, 8–11:15 a.m., Room 291

128.04, Adolescents wait rather than react impulsively when incentives are at stake
*T. TESLOVICH, **B. J. CASEY**; Dept. of Neurosci., Weill Cornell Med. Col., New York, NY

TECHNICAL ABSTRACT: A perceptual decision task is used to show that both adolescents and adults are sensitive to incentives, but in paradoxically different ways: whereas adults are quicker to make decisions when a large reward is at stake, adolescents are slower. This behavioral pattern is paralleled by enhancement of ventral striatal activity for adolescents for larger rewards. These differential reward biases on reaction time were associated with increased dorsolateral prefrontal activity. These findings suggest that adolescents are capable of waiting rather than reacting impulsively with sufficient incentive and have implications for optimizing adolescent choice behavior in the real world.

Abstract 522.07 Summary

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Diet Appears to Impact Depression-Like Symptoms in Adolescent Rat Study

Consuming a specific omega-3 fatty acid throughout development may protect rodents from depression-like states

A rodent study shows that when sufficient amounts of docosahexaenoic acid (DHA), an omega-3 fatty acid, are in the diet from gestation through puberty, young rats are less likely to exhibit depressive-like behaviors. The rats were tested in a model of depression, and their blood was tested for biochemical signs that have been associated with depression in humans. The findings were presented at Neuroscience 2012, the annual meeting of the Society for Neuroscience and the world's largest source of emerging news about brain science and health.

"The incidence of major depression in humans jumps from approximately 4 percent at age 12-13, to 12 percent at age 16-17," said Christopher Butt, principal scientist of the neuroscience group at DSM Nutritional Products. "While additional studies are needed, this rodent study provides a starting point for investigating the potential connection between nutrition and mood disorders among human adolescents."

Omega-3 fatty acids have been reported to support better mood in adult rodents, but whether a specific omega-3, such as DHA, is important in this context had not been evaluated until now. Furthermore, the developmental effects of DHA on depressive-like behaviors have not been evaluated before. During pregnancy and nursing, DHA is transferred from the mother to her offspring. In the study, pregnant rats were fed diets that were either enriched with algal DHA or deprived of DHA during pregnancy and nursing. The male offspring were then weaned from their mother's milk and provided either a DHA-rich or DHA-deficient diet.

Researchers assessed the offspring's escape behaviors during a forced swim test both before and after puberty. Blood samples were then tested for brain chemicals associated with depression. Data were obtained from 16 animals from each of the four study arms at both time points.

The study found that after puberty, depressive-like behavior and its associated biomarkers were worse in DHA-deficient offspring compared with animals given sufficient levels of DHA throughout life.

Research was supported by DSM Nutritional Products and was performed in-house at DSM using DSM's algal oil.

Scientific Presentation: Tuesday, Oct. 16, 8–10:45 a.m., Room 273

522.07, Dietary supplementation with DHA improves depression-like behaviors that emerge during puberty
*M. J. WEISER, A. E. GARRISON, **C. M. BUTT**, N. SALEM, Jr.; Neurosci., DSM, Boulder, CO; Neurosci., DSM, BOULDER, CO; Neurosci., DSM, Columbia, MD

TECHNICAL ABSTRACT: Docosahexaenoic acid (DHA) is an important omega-3 polyunsaturated fatty acid that is implicated in neurodevelopment, and it is acquired during gestation and lactation by way of maternal transfer to the offspring. Although sufficient omega-3 intake has been associated with better mood in adult rodents, it is unknown whether DHA specifically influences affective behavior in the offspring when DHA is provided through the maternal diet or in the post-weaning diet.
We sought to address these questions by 1) feeding pregnant rats with diets sufficient or deficient in DHA during gestation and lactation, 2) weaning their male offspring to diets that were sufficient or deficient in DHA, and 3) assessing depression-related behaviors (forced swim test) and plasma biomarkers (BDNF, serotonin, and melatonin) in the offspring before and after puberty.
No dietary effects were detected when the offspring were evaluated before puberty. In contrast, after puberty depressive-like behavior and its associated biomarkers were worse in DHA-deficient offspring compared to animals with sufficient levels of DHA. Post-pubertal offspring whose mothers were fed sufficient levels of DHA and were then maintained on a DHA-sufficient diet after weaning exhibited lower passive coping behavior (immobility), higher active coping behavior (climbing), and higher plasma levels of BDNF, serotonin, and melatonin than DHA-deficient offspring. Furthermore, in post-pubertal offspring whose mothers were fed a DHA-deficient diet, DHA supplementation after weaning improved active coping behavior and plasma melatonin, but it did not improve passive coping behavior or plasma BDNF and serotonin. These findings suggest that maintaining sufficient DHA levels throughout development may increase resiliency to emotional stressors and decrease susceptibility to mood disorders that commonly arise during adolescence.

Abstract 128.11 Summary

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Brain's Reward System Fails to Pull Together in Adolescent Depression

New evidence of how experience, behavior, and brain function develop together to impact depression

Depression in late-adolescent boys appears associated with changes in the coordinated functioning of two key parts of the brain's reward system, according to a first-time finding presented at Neuroscience 2012, the annual meeting of the Society for Neuroscience and the world's largest source of emerging news about brain science and health.

Researchers have previously suggested that adolescent changes in the brain's reward system play a critical role in the development of depression, as a muted pleasurable response to rewards may set the brain up for depression. The current study, led by Ericka Forbes, PhD, at the University of Pittsburgh School of Medicine, zeros in on precise parts of the brain that appear to lose their ability to function well together. The study also found possible connections between early mother-child emotional behavior and later reward system function.

The researchers followed the development of 113 boys from age 10 to age 20. Over the years, they assessed the boys for clinical depression (at ages 12, 15, and 20). They also observed parent-child interactions at ages 10, 11, and 12. Then, at age 20, they assessed neural response to reward using functional magnetic resonance imaging during a monetary reward task.

For those boys who had been depressed at any point in their lives, two key parts of the reward system had developed a strong, opposite association: when the ventral striatum, the area of the brain associated with reward motivation and pleasure, was less responsive, the medial prefrontal cortex, which regulates reward signaling, was more responsive. When considering emotional development, the researchers found that those boys who had warmer relationships with their mothers at ages 10 and 12 had an increased amygdala response to reward at age 20.

"These findings demonstrate the value of studying adolescent neural response to reward along with early development to understand how experience, behavior, and brain function develop together," Forbes said.

Research was supported with funds from the National Institute on Drug Abuse and National Institute of Mental Health.

Scientific Presentation: Sunday, Oct. 14, 8–11:15 a.m., Room 291

128.11, Depression and the adolescent brain: Ventral striatal connectivity in response to reward
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TECHNICAL ABSTRACT: Adolescence is a developmental period in which neural reward circuits are undergoing dramatic changes and risk for depression rises sharply. Given that disrupted reward function has been proposed as an endophenotype of depression (Hasler et al., 2004), developmental neuroscience models have postulated that adolescent changes in neural reward systems play a critical role in the etiology and pathophysiology of this disorder (Davey et al., 2008). While altered responding to reward in the striatum and medial prefrontal cortex (mPFC) has been consistently associated with depression (Forbes & Dahl, 2012), the functional association between these regions has not been investigated directly. Furthermore, while brain-behavior investigations have revealed correlations between function in these regions and positive affect, the association of adolescent neural response to reward with affective development has not been examined. As part of a longitudinal study of risk for psychopathology, we examined whether functional connectivity between the ventral striatum and the mPFC was associated with a history of depression and with earlier positive affect behavior. Participants were 113 male 20-year-olds (52% European-American, 40% African American, 8% other), 18 with a history of depression. Neural response to reward was assessed at age 20 using functional magnetic resonance imaging in a Siemens Trio 3T scanner during a monetary reward task. Imaging data were preprocessed in Statistical Parametrical Mapping 8 (SPM8) and analyzed using psychophysiological interaction (PPI) in SPM8, with the ventral striatum as seed region. Depression was assessed using the Kiddie Schedule for Affective Disorders and Schizophrenia (Kaufman et al., 1997) at age 12 and 15 and the Structured Clinical Interview for DSM-IV-TR (First et al., 2002) at age 20. Positive affect was observed during parent-child interactions at ages 10, 11, and 12. History of depressive disorder was associated with greater negative functional connectivity between the ventral striatum and the mPFC (313 voxels, $t = 4.28$, $p < .001$, [8, 55, -8]) during reward outcome. Positive affect at age 10 and 12 was correlated with neural response to reward at age 20. Additional analyses will explore the association between behavior at ages 10-12 and functional connectivity at

age 20. Our results underscore the importance of longitudinal designs for understanding the developmental neuroscience of affective disorders. By examining behavior and depression in relation to brain function up to 10 years later, we were able to place the possible blunting of striatal response, a neural mechanism of depression, into a developmental context.

Abstract 908.02 Summary

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There's No Place Like Home

Early home environments influence architecture of brain's outer layer in late adolescence

The number of books in a home and the way a parent addresses a child help paint a picture of childhood experience, in all its variation. Now, new findings based on a decades-long study show that variation in experience may alter brain structure in adulthood. The findings were presented at Neuroscience 2012, the annual meeting of the Society for Neuroscience and the world's largest source of emerging news about brain science and health.

The study by lead author Brian Avants, PhD, at the University of Pennsylvania, found that the degree of cognitive stimulation in the home predicted the thickness of certain regions of the cortex, the brain's outer layer. The effect was independent of mothers' intelligence, as well as the degree of parental nurturance. In addition, experience at age four had a bigger impact than experience at age eight, indicating that early life is truly a developmentally sensitive period.

The study was based on a group of children followed for more than 20 years. The research team visited the homes of the children when they were four and eight years old, and conducted detailed observational evaluations. More than 10 years later, the team used neuroimaging to collect detailed brain images of the participants. Then Avants used computational anatomy to extract images of cortical thickness that could be related to the analyses of the children's early home environment. The results showed that childhood home environment predicts frontal and temporal cortical thickness in the young adult brain.

"These findings underscore the human brain's sensitivity to its early environment," Farrah said. "They provide powerful evidence that even relatively minor variations within the normal range of home experience can affect brain development over a lifetime."

Research was supported by the National Institute on Drug Abuse and National Institute of Mental Health.

Scientific Presentation: Wednesday, Oct. 17, 2–3 p.m., Hall F-J

908.02, Early childhood home environment predicts frontal and temporal cortical thickness in the young adult brain
*B. AVANTS, L. BETANCOURT, J. GIANNETTA, G. LAWSON, J. GEE, **M. FARAH**, H. HURT; Philadelphia, PA; Children's Hospital of Philadelphia, Philadelphia, PA; Univ. of Pennsylvania, Philadelphia, PA

TECHNICAL ABSTRACT: *Introduction*: Evidence from animal models suggests that the early environment has long-term consequences on later cognitive functioning and brain development. Little work has been performed in human subjects to test whether normal variation in early experience has measurable long term effects on the brain [1,2].
Methods: Our analysis leverages 64 participants from a low socioeconomic status background who were followed from birth and who underwent T1 and diffusion tensor (DT) MR imaging on a Siemens 3T Trio. Each subject underwent the HOME assessment at age 4. MRI was collected later in life in both 29 male (a.a. = 19.4 ± 1.17) and 35 female (a.a. = 19.1 ± 1.30) subjects. Differences in the age of the cohort distribution and in parental IQ between males and females are not significantly different. Each subject also underwent the HOME assessment at age 4 which is a questionnaire that may be used to quantify a more cognitively stimulating and emotionally supportive home. In this work, we use neuroimaging and machine learning-based statistics to efficiently test the hypothesis that networks supporting cognition should be enhanced by increased stimulation and nurturance during childhood. Our statistical model, implemented in the R programming language, controls for age, gender and parental IQ.
Results and Discussion: Our results show, for the first time, that cortical thickness in early adulthood is reduced (independently from parental IQ) by increased quality of the home environment at age 4. These results, which identify a novel network of cortical regions that are directly influenced by parental behavior, appear in Figure 1. A further analysis revealed that the temporal lobe regions are related to verbal comprehension as measured near the time of imaging. This is one of the few studies to confirm the effect of normal variability in the home on neuroanatomy.

[1] van Praag H et al Nat Rev Neurosci 1: 191–198.
[2] Duncan GJ et al Child Dev 65: 296–318.

Abstract 128.02 Summary

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Social Brain Shapes Up During Adolescence

As social lives and challenges change, so too does the social brain

Regions of the social brain — those parts of the brain that help one understand other people's intentions, beliefs, and desires — continue to develop structurally across adolescence and into adulthood, according to new findings presented at Neuroscience 2012, the annual meeting of the Society for Neuroscience and the world's largest source of emerging news about brain science and health.

The study used data from the longest ongoing longitudinal neuroimaging study of human brain maturation to investigate how gray matter changed in the social brains of 288 individuals who had each undergone multiple brain scans between the ages of 7 and 30 years. The results showed that each region within the social brain undergoes substantial changes in gray matter volume during adolescence. Gray matter consists of brain cell bodies and connections between neurons (synapses), and is where communication between brain cells takes place.

"Adolescents undergo profound changes in social awareness and social interaction, and so do their social brains," said lead author Kathryn Mills from the Institute of Cognitive Neuroscience. "We now see structural changes in the social brain that accompany teens' acquisition of new social skills."

The study focused on four social brain regions: the medial prefrontal cortex (mPFC), temporoparietal junction (TPJ), posterior superior temporal sulcus (pSTS) and anterior temporal cortex (ATC). It found that the volume of gray matter, as well as its thickness, decreased from childhood into the early twenties in the mPFC, the TPJ, and the pSTS. The ATC increased in gray matter volume later into adolescence, and then decreased again. In all social brain regions, males displayed greater gray matter volumes than females.

The researchers note that the ongoing development of the social brain during adolescence may help give young people the flexibility they need to successfully navigate the changes they inevitably encounter in the social environment.

Research was supported with funds from the National Institutes of Health and the Royal Society.

Scientific Presentation: Sunday, Oct. 14, 8–11:15 a.m., Room 291

128.02, Structural changes in the social brain across adolescence
***K. L. MILLS**, F. LALONDE, L. CLASEN, J. N. GIEDD, S. J. BLAKEMORE; Inst. of Cognitive Neurosci., London, United Kingdom; Natl. Inst. of Mental Hlth., Bethesda, MD

TECHNICAL ABSTRACT: Social cognition provides humans with the necessary skills to understand and interact with one another, and is associated with a network of brain regions referred to as the social brain. These consist of: medial prefrontal cortex (mPFC; Brodmann Area 10), temporoparietal junction (TPJ), posterior superior temporal sulcus (pSTS) and anterior temporal cortex (ATC). How these specific regions develop across adolescence is not well established. The current study examined the structural developmental trajectories of social brain regions in the longest ongoing longitudinal neuroimaging study of human brain maturation. Structural trajectories of gray matter volume, cortical thickness and surface area were analyzed using surface-based cortical reconstruction software and mixed modeling in a longitudinal sample of 288 participants (ages 7-30 years, 857 total scans).
Results indicated that regions of the social brain undergo significant changes in cortical thickness, surface area and gray matter volume across adolescence. Gray matter volume and cortical thickness in medial Brodmann Area 10, TPJ and pSTS decreased from childhood into the early twenties. The ATC increased in gray matter volume until mid-adolescence, and in cortical thickness until the early twenties. Surface area for each region followed a cubic trajectory, peaking in early or pre-adolescence before decreasing into the early twenties. Differences in gray matter volume and surface area, but not in cortical thickness, were observed between female and male participants, with males displaying larger cortical volumes and greater surface area than females across all regions of interest. These results are discussed in the context of developmental changes in social cognition across adolescence.