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Press Room, Oct. 13–17: (504) 670-4630

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STUDIES REPORT EARLY CHILDHOOD TRAUMA TAKES VISIBLE TOLL ON BRAIN; CHANGES FOUND IN REGIONS CONTROLLING HEART AND BEHAVIOR

Impact on cognition, and on physical and mental health, often lasts into adulthood

NEW ORLEANS — Trauma in infancy and childhood shapes the brain, learning, and behavior, and fuels changes that can last a lifetime, according to new human and animal research released today. The studies delve into the effects of early physical abuse, socioeconomic status (SES), and maternal treatment. Documenting the impact of early trauma on brain circuitry and volume, the activation of genes, and working memory, researchers suggest it increases the risk of mental disorders, as well as heart disease and stress-related conditions 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.

Today's findings show:

- Physical abuse in early childhood may realign communication between key "body-control" brain areas, possibly predisposing adults to cardiovascular disease and mental health problems (Layla Banihashemi, PhD, abstract 691.12, see attached summary).
- Rodent studies provide insight into brain changes that allow tolerance of pain within mother-pup attachment (Regina Sullivan, PhD, abstract 399.19, see attached summary).
- Childhood poverty is associated with changes in working memory and attention years later in adults; yet training in childhood is associated with improved cognitive functions (Eric Pakulak, PhD, abstract 908.04, see attached summary).
- Chronic stress experienced by infant primates leads to fearful and aggressive behaviors; these are associated with changes in stress hormone production and in the development of the amygdala (Mar Sanchez, PhD, abstract 691.10, see attached summary).

Another recent finding discussed shows that:

- Parent education and income is associated with children's brain size, including structures important for memory and emotion (Suzanne Houston, MA, see attached speaker's summary).

"While we are becoming fully aware, in general, of the devastating impact that early life adversity has on the developing brain, today's findings reveal specific changes in targeted brain regions and the long-lasting nature of these alterations," said press conference moderator Bruce McEwen, PhD, from The Rockefeller University, an expert on stress and its effects on early brain development. "In doing so, this research points not only to new directions for the improved detection and treatment of resulting cognitive impairment, mental health disorders, and chronic diseases, but also emphasizes the importance of preventing early life abuse and neglect in the first place."

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:

Nanosymposium: **Early Life Stress and Behavioral Development**
Saturday, Oct. 13, 1–4 p.m., Room 393

Public Advocacy Forum: **The Developing Brain: How Research and Advocacy is Shaping Public Policy**
Tuesday, Oct.16, 3–5 p.m., Room 286
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Abstract 691.12 Summary

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Time Doesn't Heal All Wounds: Effects of Childhood Abuse Seen in Adult Stress Responses

"Body-control" brain regions may promote stress as result of early abuse

Physical abuse during childhood may alter the way the brain responds to even mild stress in adulthood, according to a new study. It found that early abuse is associated with an altered response of "body-control" brain areas to stress, including a shift in communication between two brain regions that integrate stress responses. 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, led by author Layla Banihashemi, PhD, measured the brain and cardiovascular activity of 155 healthy adults while they performed mildly stressful tasks inside a functional magnetic resonance imaging (fMRI) scanner. These measures were examined along with participants' reports of childhood physical abuse. Individuals who reported abuse had greater changes in blood pressure and diminished activity in "body-control" brain areas when engaged in the tasks.

"Body-control" areas of the brain regulate the function of internal organs such as the heart and the hormonal response to stress. These brain areas include the paraventricular nucleus of the hypothalamus and the bed nucleus of the stria terminalis, which normally communicate in tandem to integrate the body's stress response. However, the two brain areas responded even more in lock-step in individuals who had suffered child abuse, which may lead to enhanced stress responses.

"People who show large, stress-induced changes in blood pressure are at an increased risk of cardiovascular disease and accompanying emotional disorders," Banihashemi said. "Altered stress responses of 'body-control' brain regions in individuals with a history of abuse may contribute to this heightened vulnerability to physical and mental health problems."

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

Scientific Presentation: Tuesday, Oct. 16, 4–5 p.m., Hall F-J

691.12 , Childhood physical abuse correlates with adulthood hypothalamic and limbic forebrain activity and connectivity in response to psychological stress
*__L. BANIHASHEMI__, L. K. SHEU, P. J. GIANAROS; Psychiatry, Univ. of Pittsburgh, Pittsburgh, PA

TECHNICAL ABSTRACT: Early life experience differentially shapes later stress reactivity, as evidenced by studies in both animals and humans. However, early experience-related changes in the structure and function of neural circuits that control stress responses have not been well characterized, particularly in humans. The paraventricular nucleus of the hypothalamus (PVN) is critical in integrating autonomic and neuroendocrine stress responses. The bed nucleus of the stria terminalis (BNST), central nucleus of the amygdala (CeA), and medial prefrontal cortex (mPFC), modulate PVN activity and are themselves preautonomic structures. Thus, these hypothalamic and limbic forebrain regions form a core stress-responsive circuit. Postnatal maternal separation in rat models alters the later structure and stress-induced activation of these circuits, providing evidence that they can be influenced by early experience (Banihashemi et al. 2011, Nrosci 192:413). The goal of the present study is to translate such findings from animals to humans using neuroimaging. Here we examine how physical abuse in childhood relates to adulthood stressor-evoked activity within homologous brain regions. Participants were 155 mentally and physically healthy adults (30-50 yrs, 77 women). To evoke acute states of mental stress, participants engaged in fMRI-adapted versions of the multi-source interference (MSIT) and Stroop tasks with performance titration to ~50% accuracy and simultaneous monitoring of mean arterial pressure (MAP) and heart rate. Changes in brain activation were assessed between incongruent (stress-inducing) and congruent task conditions. Participants also completed the Childhood Trauma Questionnaire, providing a measure of childhood physical abuse. Analyses included multiple regressions controlling for several covariates, including age, gender, and childhood socioeconomic position. Childhood physical abuse correlated positively with stressor-evoked changes in MAP from baseline to the incongruent condition (B=0.59, p=0.03), and negatively with unbiased, a priori extractions of fMRI BOLD signal change values within the subgenual anterior cingulate cortex (sgACC), BNST, CeA, and PVN (B: -0.06 to -0.04, *p*: 0.001 to 0.01). Moreover, psychophysiologic interaction (PPI) analyses revealed a correlation between physical abuse and stressor-evoked BNST-PVN functional connectivity *p*=0.01). Thus, childhood physical abuse is a predictor of adulthood stressor-evoked activity within hypothalamic and limbic forebrain regions, which may mediate altered cardiovascular reactivity and vulnerability to physical and mental health.

Abstract 399.19 Summary

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Study in Rat Pups Finds Maternal Bond Trumps Learning Fear

Changes in the amygdala may prevent pups from learning fear when in mothers' presence

New work with a rodent animal model illustrates that during a critical transition period from dependency to independence, a mother's presence can regulate the way genes are activated in the pup's brain, potentially controlling sensory processing and learning. 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.

In a study led by Regina Sullivan, PhD, of New York University School of Medicine and Nathan Kline Institute, two-week-old rats were exposed to pain paired with an odor. Some of the pups had their mothers with them, others were alone. As would adult rats, pups that were alone quickly learned to fear the odor, a process dependent on the amygdala, a brain area central to emotional learning. But pups with their mothers learned to prefer the odor. They acquire this paradoxical preference as the mother's mere presence prevents the normal function of the amygdala. Meanwhile, brain circuitry that strengthens attachment to the mother appears activated, leading the pup to prefer the odor. Since rodents are housed with and reared solely by their mothers in the laboratory, maternal bonds are studied as a model of parental behaviors.

To understand the genetics at work, the researchers analyzed the amygdalae from both groups of pups — those who had been with their mothers and those who were alone when exposed to the paired odor and pain. Comparing the patterns of gene expression in the amygdalae, they found that a mother's presence was associated with changes in gene expression, particularly those related to dopamine receptors. Since dopamine is critical for learning-related changes in the amygdala, this suggests a specific pathway for the mother's ability to "turn off" the amygdala and the pups' fear. The mother's presence also alters gene expression related to immune function, although the significance is not yet clear.

"These shock-related preferences and amygdala suppression are carried into adulthood," said Sullivan. "Such patterns of pain within maternal attachment can generate profound effects throughout the lifespan, including amygdala depressive-like behavior."

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

Scientific Presentation: Monday, Oct. 15, 10–11 a.m., Hall F-J

399.19. Presence of the mother controls the transition between attachment and fear learning, and alters gene expression in the amygdala of infant rats
*__R. M. SULLIVAN__, G. A. BARR,; Emotional Brain Inst., NKI & NYU Sch. of Med., Orangeburg, NY; Anesthesia and Critical Care Med., Children's Hosp. of Philadelphia, Philadelphia, PA; Perelman Sch. of Medicine, Univ. of Pennsylvania, Philadelphia, PA

TECHNICAL ABSTRACT: There exists a "sensitive period' in many altricial species during which attachment to the caregiver is supported under a wide variety of conditions. This facilitated attachment is expressed as approaching the caregiver and can involve tolerance of considerable abuse to maintain contact. For example, abused children often form strong bonds to their abusive caretaker. A unique neural circuit during infancy supports this learning and is modeled in infant rats, which learn to prefer an odor paired with painful shock until postnatal day 10 (PN10). After PN10, pups conditioned alone learn to avoid the odor paired with shock. However, preference learning can be reinstated when the mother is present during conditioning via suppression of amygdala plasticity (Moriceau & Sullivan, 2006). Thus this is a transition period between the infant preference learning and the adult-like avoidance learning. Here we explored gene expression in the amygdala gene after conditioning with and without the mother to better understand mechanism of the neural suppression during this transition period. Twelve- to 14-day-old pups received odor-shock (0.5mA) pairings with or without an anesthetized mother present. Learning controls, with and without the mother, were included. The lateral or medial portions of the amygdala were removed 90 minutes after the end of training and processed for Affymetrix microarray analysis using standard methods. Behaviorally, pups conditioned with the mother learned an odor preference, whereas pups without the mother learned an aversion, as has been shown previously. Control conditioning groups did not learn. Analysis of gene expression patterns showed differential regulation of several functional clusters when the mother was present during the conditioning. The presence of the mother was associated with gene expression changes in GCRP receptors, in particular monoamines, and immune function. These functional groups included dopamine, serotonin and adrenergic receptor pathways, dendritic cell maturation and collagen related genes. Of note, many of these changes are carried forward with maturation and modify behavior in the adult.

Abstract 908.04 Summary

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Adult Brains Pay a Price for Childhood Deprivation

Training in adulthood may lessen the impacts on attention and other aspects of mental performance

Socioeconomic status in childhood may predict working memory in adulthood, with adults who grew up in greater poverty showing deficits in selective attention and language processing. However, aspects of these thought processes may be strengthened through training in childhood. These 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.

Led by Eric Pakulak, PhD, at the University of Oregon, researchers studied adults from a wide range of socioeconomic backgrounds. They tested adults for different aspects of working memory, attention, and language, and monitored electrical brain activity in response to specific tasks to analyze brain function.

The study found that adults who grew up in lower socioeconomic status (SES) environments had deficits in working memory compared with those from higher SES backgrounds. Working memory actively holds information in the mind, making it available for reasoning, comprehension, and other information processing, and is critical for most mental tasks.

Childhood SES had an impact on attention in adults — particularly a measure of sustained attention. In addition, the ability to understand meaning and grammar was higher in adults who came from more advantaged homes, with differences reflected in brain measures of language processing.

"In many countries, including the United States, a child's academic prospects are strongly predicted by parental income, occupation, and level of education," Pakulak said. "The academic disparities associated with SES are increasing, yet we have now shown they are not written in stone. We are finding that effective training can enhance brain function in children who come from disadvantaged backgrounds."

The research reported success in improving aspects of brain function for attention in children after an eight-week training program. The program includes working with parents on stress reduction strategies and working with children to train attention.

Research was supported with funds from the National Institutes of Health, and Department of Education, Institute of Education Sciences.

Scientific Presentation: Wednesday, Oct. 17, 4–5 p.m., Hall J-F

908.04, Effects of childhood socioeconomic status on cognition and related neural systems in adulthood
*__E. PAKULAK__, Y. YAMADA, A. HAMPTON WRAY, E. CAKIR, H. NEVILLE; Psychology, Univ. of Oregon, EUGENE, OR

TECHNICAL ABSTRACT: A large and growing literature documents the profound impact of lower socioeconomic status (SES) on cognitive skills and brain structures and functions in children (Hackman, Farah, & Meaney, 2010). In previous event-related potential (ERP) studies we have reported that lower SES children display reduced neural modulation by selective attention compared to higher SES children (Stevens, Lauinger, & Neville, 2009) and that neural systems supporting attention are modifiable by training (Stevens et al., 2008; Neville et al., 2011, under review). We have also reported that the relationship between SES and cognition persists into adulthood, as childhood SES predicts both native language proficiency as well as the ERP response to syntactic processing in adult native speakers (Pakulak & Neville, 2010). Here we show that this relationship extends to other aspects of cognition and to a different, more ecologically valid ERP language processing paradigm. Finally, we present preliminary evidence suggesting that certain aspects of these systems may be malleable in adults from lower SES backgrounds. Typically developing adults from a wide range of SES backgrounds were administered a comprehensive battery including measures of working memory and language and three ERP paradigms assessing selective attention and different subsystems of language. Childhood SES was significantly predictive of working memory in adulthood. Employing the same ERP measures of attention previously employed (e.g., Stevens et al., 2009), we found that adults from higher SES backgrounds showed enhanced neural modulation by selective attention to linguistic probe stimuli compared to adults from lower SES backgrounds.

Using an ERP language paradigm featuring a more ecologically valid context, we replicated and expanded our previous findings (Pakulak & Neville, 2010). Adults from higher SES backgrounds and who scored higher on standardized measures of language proficiency showed neural responses consistent with greater maturity to both semantic and syntactic violations. Finally, we provide evidence that aspects of attention are trainable in adults. We measured attention/executive function abilities of parents of lower SES children randomly assigned to either an evidence-based parenting program or one of two control groups and observed improvements in specific aspects of attention after eight weeks in the parent training program only. These results suggest that the effects of lower childhood SES on the development of multiple cognitive systems extends into adulthood, but also that such effects may be ameliorated by training in adulthood.

Abstract 691.10 Summary

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Chronic Stress of Poor Maternal Care Alters Brain Development in Infant Monkeys

Stress hormones accumulated in hair associated with fear and aggression, derailed brain development

Infant rhesus monkeys that receive poor maternal care experience chronic stress, as shown by the accumulation of cortisol in their hair and by behavior that is both more fearful and aggressive than that of their well-cared for cousins. Moreover, their amygdalae appear to develop abnormally. 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 research demonstrates the potency of early experience (particularly maternal care) in shaping the development of the brain and behavior, reported senior author Mar Sanchez, PhD, of Emory University. The Sanchez team studied mother-infant rhesus monkey pairs living in large social groups. Because cortisol accumulates in hair formed during exposure to stress, the researchers shaved the back necks of the newborn monkeys and analyzed hair that grew between birth and six months. This can be the toughest period for infants whose mothers mistreat or reject them. The researchers also examined the infants' behavior and used magnetic resonance imaging (MRI) to measure their amygdalae, the brain region responsible for intense emotion and fear.

Infant monkeys that experienced chronic stress were more likely to freeze — a fearful behavior — when confronted with an unfamiliar human intruder, and more likely to act aggressively (rather than submissively) when the intruder maintained eye contact with the animal. Additionally, the higher the cortisol accumulation, the greater the demonstrations of fear and aggression.

MRI found that animals with larger amygdalae showed more fearful and aggressive behavior at three months of age. Animals with the smallest or largest amygdalae had the highest accumulated hair cortisol.

"These findings suggest that early life stress, and its increased exposure to cortisol, affects both brain and behavioral development, contributing to the increased risk of psychopathology and behavioral disorders," Sanchez said.

Research was supported with funds from the National Institutes of Health, National Center for Research Resources.

Scientific Presentation: Tuesday, Oct. 16, 2–3 p.m., Hall F-J

691.10, Early life stress leads to increased fear and aggressive responses to threat in infant rhesus monkeys: Associations with increased cortisol and amygdala volume

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TECHNICAL ABSTRACT: Early experiences are potent modulators of brain and behavioral development. Using a nonhuman primate model of adverse experience in the form of infant maltreatment (operationalized as physical abuse and rejection by the mother during the first 3 months of life) we longitudinally investigated its effects on brain and behavioral development, and the associations between these measures. Chronic exposure to stress can be identified by measures of cortisol accumulation in hair. Using this method we have shown that infant maltreatment results in chronic early life stress in infant rhesus monkeys, evidenced by maltreated infants have approximately two-fold higher hair cortisol levels than controls from birth through 6 months of age, accumulation which occurred during exposure to maltreatment. To determine the associations of this early stress index with behavioral reactivity to threat in the infants, we examined the correlations of hair cortisol with fear and aggressive responses to the Human Intruder (HI) paradigm. The HI has 3 conditions (10 min each): alone (induces exploration and vocalizations), a profile condition in which the intruder presents his/her profile to the animal (elicits freezing, a fearful behavior), and the stare condition in which the intruder maintains eye contact with the animal (eliciting both aggressive and submissive behaviors). Our findings suggest increased freezing during profile in maltreated infants, both at 3 and 6 months, and also increased non-contact aggression (threats) and decreased submission (lipsmack) during the stare condition at all ages studied (3, 6, 12 and 18 months), in comparison to controls. A positive correlation was detected between hair cortisol accumulation from birth through 6 months and fear and aggressive responses to the HI, with higher cortisol accumulation being associated with higher levels of freezing during profile and threats during stare. We also analyzed the effects of maltreatment on brain structural development, focusing on amygdala volume and its relationship to the behavioral alterations detected during the HI. Positive correlations between amygdala volume and fear and threat behavior were detected at 3

months, but not at the other ages studied. We also detected significant correlations between accumulated hair cortisol (birth through 6 months) and amygdala volume at 3 months, which followed a U-shaped relationship. These results suggest that infant maltreatment is an early stress experience that affects the development of brain regions involved in the control of threat responses (specifically, the amygdala) during infancy, an effect that seems to be mediated by early cortisol elevations.

Speaker's Summary

Speaker: Suzanne Houston (323) 361-7347
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Parent Education and Income is Associated with Children's Brain Size (908.03)

Poster Session: Childhood Socio-Economic Status and Brain Development

Wednesday, Oct. 17, 3–4 p.m., Hall F-J

Socioeconomic disparities in childhood are associated with remarkable differences in cognitive and socio-emotional development during a time when dramatic changes are occurring in the brain. Yet, the neurobiological pathways through which socioeconomic status (SES) shapes development remain poorly understood. Behavioral evidence suggests that language, memory, social- emotional processing, and cognitive control exhibit relatively large differences across SES. Here we investigated whether volumetric differences could be observed across SES in neural regions that support these skills, including the hippocampus, the amygdala, the anterior cingulate cortex and several structures in a language-supporting network in the left temporal, temporo-occipital and frontal cortices.

Methods: Sixty typically developing, socioeconomically diverse children (31 female) were recruited, ranging in age from 5 to 17 years (Mean=11.4, SD=3.1). Participants had no history of neurological impairment, psychiatric disability, learning disability, language impairments, developmental delay, or significant exposure to prenatal teratogens such as alcohol. Two to four sagittal T1-weighted images were collected for each participant using the following parameters: TR= 1900 ms; TE= 4.38 ms; flip angle, 15; matrix size, 256x256; voxel size, 1 x 1 x 1 mm; acquisition time, 8 min 8s. Pre-processing and definition of cortical and subcortical gray matter regions on structural images were conducted using automated brain segmentation software (Freesurfer, 4.5). First, relationships between SES and regional cortical volume were explored. Next, we examined the degree to which the effects of SES factors on regional brain volume might change with age, by examining SES x age interactions in each ROI.

Results: Highly significant SES differences in regional brain volume were observed in the hippocampus and the amygdala. Specifically, higher parental education levels predicted larger amygdala volumes, whereas higher income-to-needs ratios predicted larger hippocampal volumes. In addition, SES x age interactions were observed in the left superior temporal gyrus and left inferior frontal gyrus, such that children from higher SES families showed relatively greater volumetric increases with age in these regions. These results were not explained by differences in gender, race or IQ. Likely mechanisms include differences in the home linguistic environment and exposure to stress, which may serve as targets for intervention at a time of high neural plasticity.

This research was supported by the National Institute of Child Health and Human Development and the John M. Driscoll MD Scholars Program.