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

Contacts: Kat Snodgrass, (202) 962-4090
Todd Bentsen, (202) 962-4086

THIS IS YOUR BRAIN ON FOOD: STUDIES REVEAL HOW DIET AFFECTS BRAIN FUNCTIONS

Imaging technology allows scientists to link what we eat to what (and how) we think

NEW ORLEANS — Studies released today explore the neurological component of dietary disorders, uncovering evidence that the brain's biological mechanisms may contribute to significant public health challenges — obesity, diabetes, binge eating, and the allure of the high-calorie meal. 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.

Scientists are ultimately searching for new ways to treat diet-related disorders while raising awareness that diet and obesity affect mental as well as physical health.

Today's new findings show that:

- Being obese appears to affect cognitive function, requiring more effort to complete a complex decision-making task (Timothy Verstynen, PhD, abstract 802.20, see attached summary).
- Brain images suggest that when people skip breakfast, the pleasure-seeking part of the brain is activated by pictures of high-calorie food. Skipping breakfast also appears to increase food consumption at lunch, possibly casting doubt on the use of fasting as an approach to diet control (Tony Goldstone, MD, PhD, abstract 798.02, see attached summary).
- A study in rats suggests they may be able to curb binge-eating behavior with medication used to keep substance abusers clean and sober (Angelo Blasio, PhD, abstract 283.03, see attached summary).

Other recent findings discussed show that:

- Amidst growing concern that diet-related metabolic disorders such as diabetes impair brain function, an animal study reports that a high-sugar diet may affect insulin receptors in the brain and dull spatial learning and memory skills. But omega-3 supplements may at least partially offset this effect (Rahul Agrawal, PhD, see attached summary).
- Evidence from a rat study suggests that a new compound under development to treat compulsive eating disorders and obesity may be effective at blocking a specific receptor in the brain that triggers food cravings and eating when activated by "food related cues," such as pictures or smells, irrespective of the body's energy needs (Chiara Giuliano, PhD, see attached summary).

"These are fascinating studies because they show the brain is an often overlooked yet significant organ in an array of dietary disorders," said press conference moderator Paul Kenny, PhD, of The Scripps Research Institute in Florida, an expert on addiction and obesity. "Many of these findings have the potential to lead to new interventions that can help reduce the ranks of the obese, helping those who struggle daily with dietary decisions reassert control over what they eat."

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 802.20 Summary

Lead author: Timothy Verstynen, PhD 412-624-1194
Carnegie Mellon University timothyv@andrew.cmu.edu
Pittsburgh, Penn.

Scientists Find Obesity Associated with Changes in Brain Connections

Study suggests obesity may affect how hard the brain works to process information

A new study finds that being obese appears to affect cognitive function, underscoring the important link between diet and brain health. The research was 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.

Timothy Verstynen, PhD, of Carnegie Mellon University, the study's lead author and his colleagues at the University of Pittsburgh used functional magnetic resonance imaging to image the brains of 29 adults all considered neurologically healthy, but with Body Mass Index scores that ranged from normal to obese. When compared with brain images of leaner participants the images of individuals in the overweight and obese range reflected hyper-connectivity in brain pathways that are critical to cognitive functions, suggesting reduced communication efficiency in these pathways, according to the scientists. Moreover, obese individuals also required more effort to perform a complex decision-making task.

"As people put on unhealthy amounts of weight, the body's energy systems begin to degrade and you can start to see the negative effect on brain circuitry, particularly areas that are important for controlling impulsive behaviors," Verstynen said.

Research was supported by the Defense Advanced Research Projects Agency, the Pittsburgh Claude D. Pepper Older Americans Independence Center, the University of Pittsburgh Alzheimer's Disease Research Center, and the National Institutes of Health.

Scientific Presentation: Wednesday, Oct. 17, 11 a.m.–12 p.m., Hall F-J

802.20, Altered cortico-basal ganglia connectivity with obesity predicts inefficient executive control processing
T. D. VERSTYNEN, R. LECKIE, A. WEINSTEIN, J. JACKIC, D. ROFEY, K. ERICKSON; Dept. of Psychology, Dept. of Hlth. and Physical Activity, Univ. of Pittsburgh, Pittsburgh, PA; Dept. of Psychology, Carnegie Mellon Univ., Pittsburgh, PA; Weight Mgmt. and Wellness Ctr., Univ. of Pittsburgh Med. Ctr., Pittsburgh, PA

TECHNICAL ABSTRACT: Many cognitive functions, including executive control, saliency and reward processing, share a common circuitry through the cortico-basal ganglia network. Several of these abilities have recently been shown to be impaired in individuals with chronic obesity. Obesity has also been linked to altered basal ganglia dynamics, particularly reward processing in the striatum. In this experiment we tested the hypothesis that the obesity-linked changes to cognitive processing are directly associated with dysfunctional cortico-basal ganglia dynamics. We used resting state fMRI (Siemens Verio 3T, TE=20 ms; TR=1500 ms; Flip Angle=90°, 3.2 mm x 3.2 mm x 4 mm voxels, 30 slices) to determine how increased body mass index (BMI), a common measure of obesity, is correlated with changes in the dynamics of the cortico-basal ganglia networks and how these changes correlate to cognitive processing. In otherwise neurologically healthy adults (N=29, 7 male, mean age 38 years, BMI range = 18.5=45.7) BMI correlated with global connectivity changes in bilateral regions of the orbitofrontal cortex and caudate nucleus. Using these as seed regions, we found a hyper-connectivity of reward and saliency sub-networks of the cortico-basal ganglia system, in subjects with high BMI values. Using a task-evoked fMRI paradigm, we then probed cortical dynamics during the color-word Stroop task and found that these responses were stronger in obese individuals (BMI > 30) than lean controls (BMI < 25). Most importantly, the BMI-associated changes in resting state cortico-basal ganglia connectivity predicted the exaggerated evoked responses in the Stroop task. These results highlight how obesity-linked changes to saliency and reward networks may also influence subsequent executive control processing.

Abstract 798.02 Summary

Lead author: Tony Goldstone, MD, PhD (20) 331-358-56
MRC Clinical Sciences Centre, Imperial College tony.goldstone@imperial.ac.uk
London, England

Good Breakfast and Good Diet: New Findings Support Common Sense

Brain scans of breakfast-skippers show circuits may be primed for poor eating

A new study that compared participants' brain scans and eating patterns — both after breakfast and when they are fasting —may show why eating the first meal of the day may be a good way to avoid subsequent over-eating and poor dietary choices. 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.

Scientists lead by Tony Goldstone, MD, PhD, from the MRC Clinical Science Centre at London's Imperial College, obtained multiple magnetic resonance images (MRIs) of 21 volunteers who had not eaten anything before arriving for the tests. On one visit they were first given a 750-calorie breakfast before the scans began; on another visit they received no breakfast. Lunch was always served after the scans.

"Through both the participants' MRI results and observations of how much they ate at lunch, we found ample evidence that fasting made people hungrier, and increased the appeal of high-calorie foods and the amount people ate," said Goldstone.

In the MRIs of those who had not eaten breakfast, the scientists discovered a variation in the pattern of activity in the orbitofrontal cortex — the area right above the eyes that can affect decisions regarding the pleasantness and reward value of food. The scientists reported that when fasting participants were shown pictures of high-calorie food, this brain area was "activated," a reaction less strong when they had eaten breakfast.

Moreover, Goldstone and colleagues noted their ability to use brain MRIs to predict which individuals appear primed to respond strongly to high-calorie foods. This suggests the orbitofrontal cortex may play a vital role in determining how people make dietary choices. They said the study also adds to previous research that indicates fasting may be a poor way to lose weight as it seems to create a "bias" in the brain toward seeking a high-calorie food reward.

Research was supported by the UK Medical Research Council, European Union Marie Curie Fellowship, Imperial College Healthcare Charity, and the National Institute for Health Research.

Scientific Presentation: Wednesday, Oct. 17, 9–10 a.m., Hall F-J

798.02, Salience resting state network integrity in the orbitofrontal cortex predicts task activation to viewing high-calorie foods when fasted
A.P. GOLDSTONE, C. G. PRECHTL, J. A. STARKE, S. SCHOLTZ, N. CHHINA, A. MIRAS, G. DURIGHEL, R. LEECH, D. J. SHARP, C. F. BECKMANN, G. S. FROST, J. D. BELL; Metabolic and Mol. Imaging Group, MRC Clin. Sci. Ctr., Robert Steiner MRI Unit, Computational, Cognitive and Clin. Neuroimaging Lab., Div. of Diabetes, Endocrinol. and Metabolism, Imperial Col. London, London, United Kingdom

TECHNICAL ABSTRACT: *Background*: Fasting increases appetite, food intake and hedonics, and activation of brain reward systems to food cues. Changes in brain activity in the resting state (i.e. in the absence of a task) are also functionally relevant. A number of resting state networks (RSN) have been identified including a salience network (SALN) involving the insula, ventral anterior cingulate (vACC) and orbitofrontal (OFC) cortex, regions also activated by food cues. We hypothesised that functional integrity within the SALN at rest may predict activation in the same regions during a food evaluation fMRI task and that this relationship may be influenced by food category and feeding state.
Methods: 21 healthy, non-obese subjects (16 male, mean ± SD age 25.4 ± 7.5yrs, BMI 24.1 ± 2.7 kg/m) attended after an overnight fast. After a first visit [Initial], at subsequent visits subjects either remained fasted [Fasted], or received a 730kCal breakfast at t=0min [Fed], in a randomised cross-over design. At +85min subjects had a 10min resting state fMRI scan (3T, 186 vol, TR 3sec), followed by a food picture fMRI task during which they rated the appeal of high-calorie or low-calorie foods or household objects (2x10min runs, 60 pictures each). Independent component analysis in FSL was used to identify regions of interest (ROI) within the SALN from the Initial resting fMRI scan: insula, vACC and OFC. ROIs for activation to food pictures (vs. objects) in the same sub-regions were also determined from the Initial task fMRI scan (FDR $P<0.05$). Network integrity within each SALN ROI was correlated with task BOLD activation within each ROI at the Fasted and Fed visits.

Results: Fasting increased hunger, appeal of high-calorie foods and food intake at lunch after scanning ($P<0.05$). BOLD activation to high-calorie foods was greater at the Fasted than Fed visit in the OFC ($P<0.05$), but not in the vACC or insula. At the Fasted visit, resting SALN integrity in the OFC was positively correlated with task OFC activation to high-calorie foods ($r=+0.52$, $P=0.02$). However this correlation was not significant for low-calorie foods ($r=+0.31$, $P=0.18$), nor for the vACC or insula ($P=0.30$-0.98). At the Fed visit, there were no significant correlations between resting SALN integrity and task activation for any ROI ($P=0.10$-0.89).
Conclusion: OFC network integrity at rest predicted subsequent OFC activation during a picture evaluation task for high-calorie foods. Furthermore this relationship was seen when fasted but not when fed, supporting previous work that fasting biases OFC responses towards high-calorie foods. This highlights the interaction between feeding status and OFC function in encoding reward value and salience.

Abstract 283.03 Summary

Lead author: Angelo Blasio, PhD (617) 894-9723
Boston University School of Medicine blasio@bu.edu
Boston, Mass.

Drug Used in Addiction Treatment May Block Impulse to Binge on Food

Effect on sugar-craving rats could prompt hunt for medications for diet disorder

Often portrayed as a behavior akin to drug addiction, new research in rats offers evidence that binging on junk food — a psychiatric illness that affects 15 million Americans — might be inhibited by a medication now used to help sustain recovery from alcohol and drug abuse. 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.

Lead author Angelo Blasio, PhD, of the Laboratory of Addictive Disorders at Boston University School of Medicine, and his colleagues found that when they used the drug naltrexone to block receptors in a part of the brain involved in seeking rewards and making decisions, rats curbed their excessive consumption of highly palatable foods.

"These results may open new avenues of investigation toward developing pharmacological treatments for Binge Eating Disorder in humans," Blasio said. "People who engage in this behavior often describe it as a compulsive loss of control and our work shows there may be medications that can help them regain control."

Blasio and his colleagues, including Pietro Cottone, PhD, director of the laboratory and senior author of the study, allowed a group of rats to develop into binge eaters by providing them with a chocolate-flavored, high-sugar diet for one hour every day. Within two weeks the rats were exhibiting binge-eating behavior. Meanwhile, a second group of rats was offered a normal, healthy diet. Both groups were then given naltrexone injections at two different sites in the brain.

The drug reduced the amount of food consumed in both groups, except when it was injected directly into the prefrontal cortex — an area of the brain just behind the forehead. There, the drug modified the eating behavior only of the binging rats. The researchers also discovered that the binging rats had undergone genetic changes in the proteins know as opioid receptors, which are located in the prefrontal cortex. When activated by opiates like heroin, these receptors stimulate areas of the brain involved in pleasure and reward; scientists suspect the receptors respond to certain foods in much the same way.

Research was supported by the National Institute on Drug Abuse, National Institute of Mental Health, National Institute on Alcohol Abuse and Alcoholism, and the Peter Paul Career Development Professorship.

Scientific Presentation: Sunday, Oct. 14, 3–4 p.m., Hall F-J

283.03, Title Blockade of opioid receptors in the prefrontal cortex decreases binge-like eating
A. BLASIO, L. STEARDO, V. SABINO, P. COTTONE; Pharmacol. & Exptl. Therapeut., Boston Univ. Sch. of Med., Boston, MA; Dept. of Physiol. and Pharmacol., Univ. of Rome La Sapienza, Rome, Italy

TECHNICAL ABSTRACT: Binge eating disorder is an addiction-like disorder characterized by rapid, excessive and uncontrollable food consumption of highly palatable foods, which occurs within discrete periods of time. The central opioidergic system is highly involved in the modulation of both homeostatic and hedonic feeding. Numerous studies have suggested that subcortical regions, such as the Nucleus Accumbens (NAcc), are involved in the modulation of hedonic feeding. However, the role of the opioid receptor system of the Prefrontal Cortex (PFC) in food intake is poorly understood. The present study examined the effect of opioid receptor blockade in a rat model of binge-like eating. Male Wistar rats were allowed to nosepoke to obtain either a sugary highly-palatable diet (Palatable rats) or a regular chow diet (Chow control rats) 1 hour a day, using an operant FR1 schedule of reinforcement. Following stabilization of performance, subjects were systemically administered the non-selective opioid receptor antagonist naltrexone (0.03, 0.1, 0.3 mg/kg, s.c.). Naltrexone was also microinfused in the PFC and the NAcc (10, 50 ug). Finally, differences in opioid receptors gene expression in PFC and NAcc were assessed in Palatable rats and Chow control rats, using RT-PCR. Palatable rats rapidly developed binge-like eating, escalating the 1-hour intake by 4 times. Naltrexone, administered both systemically and intra-NAcc, dose-dependently reduced responding for food in both Chow and Palatable rats. Interestingly, site-specific administration of naltrexone in the PFC reduced responding for food selectively in Palatable rats, without affecting responding in the Chow group. RT-PCR results showed differential changes in gene expression of opioid receptors in Palatable rats compared to Chow control rats. Our data suggest that neuroadaptations in the opioid receptor system of the PFC occur following intermittent access to highly palatable food, which may be responsible for the development of binge-like eating.

Speaker's Summary

Speaker: Rahul Agrawal, PhD (310) 825-1788
University of California, Los Angeles ragrawalcdri@rediffmail.com
Los Angeles, Calif.

Metabolic Syndrome in the Brain: How the Balance between Sugars and Omega-3 Fatty Acid Determines Cognitive Plasticity (726.13)

Nanosymposium Session: Metabolism and Brain Function
Wednesday, Oct. 17, 8–11:15 a.m., Room 288

There is growing concern that high sugar consumption is a causative factor for the rise of metabolic syndrome (MetS), the collection of obesity-related risk factors associated with insulin resistance. The concept of MetS has mostly been associated with the body; here we provide novel evidence for the consequences of metabolic disturbances on brain function. Metabolic disorders such as diabetes and obesity increase the vulnerability to mental illness; however, the mechanisms that link cellular metabolism and mental health are poorly understood. We induced metabolic syndrome by high fructose intake (15%) in drinking water and assessed the capacity of dietary n-3 fatty acids (deficient Vs 1.2% DHA) to modulate the vulnerability for MetS. The peripheral occurrence of MetS was confirmed by an increase in insulin resistance index, insulin and triglycerides levels in blood. The effects of MeS in brain were expressed by a decrease in hippocampal insulin receptor signaling in fructose treated animals exposed to the n-3 deficient diet. These changes were concurrent with reductions in memory functions in Barnes maze test. The same dietary treatment resulted in disruption of membrane homeostasis as evidenced by an increase in levels of the lipid peroxidation marker 4-hydroxynonenal (4-HNE), and an increase in ratio of n-6/n-3. A disturbance in energy metabolic pathways was manifested by a reduction in AMPK and LKB1 phosphorylation as well as a decrease in Sir2 levels. The changes observed in LKB1 phosphorylation varied in direct proportion to the n-3 fatty acid docosohexaenoic (DHA) level, and in inverse proportion to the level of the n-6 fatty acid arachidonic (AA), suggesting that a decline in the ratio n-6/n-3 contributes to maintain energy homeostasis. The promoting effect of the fructose/DHA deficiency on dysfunctional synaptic plasticity was evidenced by a decrease in phosphorylation of CREB, synapsin I and a synaptophysin (SYP) levels. The deficiency of dietary n-3 increases vulnerability to impaired cognitive functions and intake of high fructose diet exacerbates this condition. It is encouraging that the presence of n-3 diet was sufficient to buffer the effects of metabolic dysfunction. This study provides a potential mechanism for the deleterious effects of high sugar diets on cognitive function and the possibility to counteract these effects via other healthy components in the diet such as DHA.

Speaker's Summary

Speaker: Chiara Giuliano, PhD 44 (776) 050-5405
University of Cambridge Cg451@cam.ac.uk
Cambridge, England

Attenuation of Highly Palatable Food, Heroin and Cocaine Seeking By GSK1521498, a Novel μ-Opioid Receptor Antagonist, Compared to Naltrexone (362.08)

Poster Session: CNS Depressants, Neuropeptides, and Behavior
Monday, Oct. 15, 11 a.m.–12 p.m., Hall F-J

Evidence has implicated the endogenous opioids and in particular μ-opioid receptors in emotional behaviour, memory and the regulation of reward circuits, especially in the context of heroin addiction and hedonic responses to ingestive rewards. The μ-opioid receptor antagonist naltrexone (NTX) has been reported to be effective in preventing relapse to alcoholism and in reducing alcohol and cocaine craving during abstinence. The aim of the present experiments was to investigate the effects of a novel selective μ-opioid receptor antagonist GSK1521498 on food, cocaine and heroin seeking and the primary reinforcement of self-administration behaviour. Rats were first trained to self-administer food, or cocaine, or heroin and then to seek the reward over prolonged periods of time under a second-order schedule of reinforcement, in which responding is maintained by contingent presentation of a reward-associated conditioned reinforcer. After stable seeking behaviour had been acquired, animals were treated with either GSK1521498 (0.1, 1 and 3mg/kg; IP) or naltrexone (NTX 0.1, 1 and 3mg/kg; SC) before each test session. GSK1521498 dose-dependently reduced food seeking both before and after food ingestion, whereas NTX reduced food seeking only after food ingestion. Thus, whilst both drugs affected the post-ingestional value of the preferred food, GSK1521498 also directly decreased incentive motivation for chocolate. In addition, cocaine seeking was dose-dependently decreased following GSK1521498 treatment. However, the same treatment had no effect on cocaine self-administration under a continuous reinforcement schedule. Treatment with NTX had a less pronounced, but similar effect. GSK1521498, but not NTX, also dose-dependently reduced heroin seeking both before and after infusion of the drug although both increased heroin self-administration under continuous reinforcement. These data suggest that GSK1521498, by reducing opioid transmission at the μ-opioid receptor, may have therapeutic potential to reduce maladaptive, palatability-driven eating behaviour, but also the propensity to seek cocaine or heroin. In addition, it may diminish the consequence of an initial relapse to heroin taking.