ESCoNS

FIRST ANNUAL MEETING

September 19 & 20, 2011

UCSF Mission Bay Conference Center

Dear Colleagues,

Welcome to the first meeting of ESCoNS! We are so pleased that you have joined us for two days of exciting scientific talks, poster presentations, and networking.

The idea for ESCoNS emerged just last November when George Rose, Chief Public Policy Officer for Activision/Blizzard, came to meet with me at the urging of Garen Staglin, a philanthropist and tireless advocate for mental health research (and also co-founder of IMHRO, the International Mental Health Research Organization). George was interested in exploring ways in which the huge technological advances in the entertainment software industry could be harnessed for the public good; Garen had told him about my research investigating computerized cognitive training exercises for schizophrenia.

I explained to George that a small handful of clinical investigators around the world were studying how computerized "video game like" training could improve impaired brain functioning in a number of clinical conditions, but that the science was still in its infancy. This emerging research area needed a forum where scientists could meet and share their data; the goal would be for us to work together to develop a neuroscientifically-informed and empirically-based approach to an entirely new field of cognitive neurotherapeutics.

George got it immediately, and as a good businessman, he took it one step further. He said that it wasn't enough to simply develop a new treatment approach for mental and neurological disorders using computerized cognitive training—the new approach had to be developed in the context of the powerful, engaging, and scalable technology developed by the entertainment software industry. "Pedaling on a stationary bike is good for your health", he said. "But pedaling a stationary bike to great music with your friends in a Spinning class is fun and keeps you motivated!" And so ESCoNS was born. Adam Gazzaley and Mor Nahum immediately and enthusiastically joined us to form our local organizing committee; Daphne Bavelier, Torkel Klingberg, and Takeo Watanabe graciously and generously agreed to serve as a Scientific Advisory Committee. The result is the fabulous program that will unfold over the next 2 days.

As a registered attendee at this first meeting of ESCoNS, you are now a member of our fledgling society. We hope you will find the science and the ideas presented here as exciting as we do. Please actively join in the conversations, and please help us to discover ways of moving this field forward with a vision that includes both scientific rigor and real-world dissemination—for our ultimate goal is, of course, to create meaningful improvement in the lives of those who suffer from brain disorders.

Sophia Vinogradov

SCIENTIFIC ADVISORY COMMITTEE

Sophia Vinogradov, M.D.,
Professor of Psychiatry, UCSF

Takeo Watanabe, Ph.D.,
Professor of Neuroscience, Boston University

Adam Gazzaley, M.D., Ph.D.,
Associate Professor of Neurology, Physiology and Psychiatry; Director, Neuroscience Imaging Center, UCSF

Torkel Klingberg, M.D., Ph.D.,
Professor of Cognitive Neuroscience, the Stockholm Brain Institute, Karolinska Institute, Sweden

Daphne Bavelier, Ph.D.,
Professor, Brain & Cognitive Sciences, Centers for Visual Sciences, and Language Studies; Director, MindSpace Virtual Reality Laboratory, University of Rochester

AGENDA

MONDAY, SEPTEMBER 19, 2011

7:30 am — Registration & Check-In

7:15 am — Continental Breakfast *in the Foyer*

8:15 – 8:30 am — Greeting & Introductions by **Sophia Vinogradov, George Rose** and **Adam Gazzaley**

8:30 – 10:00 am — **Plasticity in Neural Systems**

Chair: **Takeo Watanabe**

8:30 am **Michael Silver**, University of California, Berkeley
Learning-based plasticity in visual systems

9:00 am **Michael Kilgard**, University of Texas at Dallas
Directing neural plasticity to understand and treat neurological disease

9:30 am **Takeo Watanabe** and **Yuka Sasaki**, Boston University
Roles of attention and reward in perceptual learning

10:00 am **Merav Ahissar**, The Hebrew University of Jerusalem
Perceptual learning and cognition

10:30 – 11:00 am — Coffee Break *in the Foyer*

11:00 am – 12:30 pm — Panel Discussion

Translating Neuroscience into Marketable Therapeutic Interventions
Part 1: From Research Findings to Business Plan

Chair: **George Rose**, Activision

Uri Polat, Ucansi Inc. and Tel-Aviv University — Taking a clinically proven treatment and developing a commercial product

Adam Haim, Division of Services and Intervention Research (DSIR) – NIMH The Small Business Innovation Research (SBIR) Program — NIH funding for academia-industry partnerships

Laird Malamed, Activision — Game development

Dan Dardani, MIT — Technology transfer

Henry Mahncke, Posit Science and Brain Plasticity Institute — Regulatory and reimbursement issues

Alvaro Fernandez, SharpBrains Market Research — Survey of emerging needs, markets and policies

Alice Medalia, Columbia University — Consumer preferences

Jessica Lindl, Scientific Learning, Inc. — Marketing therapeutic interventions for children

12:30 – 2:00 pm — Buffet Lunch *outside on the **Bank of America** patio*

2:00 – 5:00 pm — **Demonstrating Meaningful Neural Plasticity in Humans**

Chair: **Adam Gazzaley**

2:00 pm **Mark D'Esposito**, University of California, Berkeley
Training-induced changes in functional connectivity in frontal cortex

2:30 pm **John Jonides**, University of Michigan
Improving fluid intelligence via cognitive training

3:00 pm **Adam Gazzaley**, University of California, San Francisco
Multimodal imaging of neural plasticity after training

3:30 pm — Coffee Break *in the Foyer*

4:00 pm **Molly Wagster**, NIA, NIH
The NIH ToolBox

4:30 pm **Cameron Carter**, University of California, Davis
Translating tasks from Cognitive Neuroscience into biomarkers of treatment response: The CNTRICS perspective

5:15 – 7:30 pm — Poster Session and Cocktail Reception, wine generously sponsored by **Staglin Family Vineyard**.

AGENDA

TUESDAY, SEPTEMBER 20, 2011

7:30 am — Registration & Check-In

7:15 am — Continental Breakfast *in the Foyer*

8:15 – 8:30 am — Greeting & Introductions by Sophia Vinogradov, George Rose and Adam Gazzaley

8:30 am – 12:15 pm — **Neural Plasticity and Cognitive Training in Impaired Individuals Across the Lifespan**

Chair: **Torkel Klingberg**

- 8:30 am **Torkel Klingberg**, Karolinska Institute
  Working memory training in children with attention deficits
- 9:00 am **Yair Bar-Haim**, Tel Aviv University
  Computerized training for anxiety disorders in children
- 9:30 am **Nina Kraus**, Northwestern University
  Music and software-based training for the development and maintenance of communication skills

10:00 am — Coffee Break *in the Foyer*

- 10:30 am **Sophia Vinogradov**, University of California, San Francisco
  Computerized cognitive training in schizophrenia
- 11:00 am **Wayne Gordon** and **Joshua Cantor**, Mount Sinai School of Medicine
  Cognitive training for Traumatic Brain Injury
- 11:30 am **Karlene Ball**, University of Alabama at Birmingham
  Age-related cognitive decline, cognitive training, and transfer to everyday performance

12:30 – 2:00 pm — Box Lunch in the Robertson Auditorium: *seating is also available outside on the* ***Bank of America*** *patio*.

12:30 – 1:45 pm — Panel Discussion
Translating Neuroscience into Marketable Therapeutic Interventions
Part 2: From Product to Consumer

See details on Monday schedule.

2:00 – 5:00 pm — **Future Directions and Future Innovations**

Chair: **Daphne Bavelier**

- 2:00 pm **Daphne Bavelier**, University of Rochester
  How can we promote learning to learn? Action video games as exemplary learning tools
- 2:30 pm **Alvaro Pascual-Leone**, Harvard University
  How can we combine brain stimulation techniques with cognitive training?
- 3:00 pm **Jim Blascovich**, University of California, Santa Barbara
  How does immersive VR influence brain motivational systems?

3:30 pm — Coffee Break *in the Foyer*

- 4:00 pm **Michael Merzenich**, University of California, San Francisco, Brain Plasticity Inc.
  Is there any limit to the range of neurological disorders that can respond to computerized training?
- 4:30 pm **Paula Tallal**, Rutgers University
  Making cognitive training effective, engaging and viral: What can scientists and the gaming industry learn from each other?
- 5:00 pm **Alan Gershenfeld**, E-Line Media
  What will be the social impact of harnessing games for brain health?

5:30 – 6:00 pm — Closing Remarks by **Sophia Vinogradov, George Rose** and **Adam Gazzaley**

Monday, September 19, 8:30 am – 10:30 am

PLASTICITY IN NEURAL SYSTEMS

Chair: Takeo Watanabe

Speakers:

Michael Silver

Michael Kilgard

Takeo Watanabe

Yuka Sasaki

Merav Ahissar

ABSTRACTS

Learning-based plasticity in visual systems. Michael A. Silver. University of California, Berkeley - I will present an overview of learning-based plasticity in vision, focusing on visual perceptual learning and its neurophysiological and neurochemical substrates. Perceptual learning is a long-lasting form of plasticity that is often specific to the particular stimulus features used for training. Several studies have shown that the neurotransmitter acetylcholine can facilitate experience-dependent neural plasticity. My laboratory has found that enhancing cholinergic transmission with the cholinesterase inhibitor donepezil (trade name: Aricept) increases the magnitude and specificity of visual perceptual learning in healthy humans. These results will be discussed in the context of perceptual learning-based treatments of amblyopia.

Directing Cortical Plasticity to Understand and Treat Neurological Disease. Michael P. Kilgard, Professor of Neuroscience, University of Texas at Dallas - Even simple experiences activate large numbers of neurons in the central nervous system. It is not at all clear how many neurons are needed to generate a sensory percept or how activity among these neurons leads to useful behavior. Training-induced map plasticity seems to suggest that many neurons contribute to the perception of even simple stimuli. Our recent demonstration that map plasticity aids discrimination learning but is not needed for accurate discrimination (Neuron, 2011) suggests that a new model of brain function is needed. In the Expansion-Renormalization Model large numbers of neurons are engaged during the early stages of learning so that a subpopulation of neurons that is most effective in performing the task can be identified. This new selectionist model makes specific predictions that can be tested with available molecular techniques. The model also predicts that small numbers of neurons could generate phantom percepts such as chronic pain and tinnitus, which might be reversed using large scale plasticity. Pairing brief pulses of vagus nerve stimulation (VNS) with tones is sufficient to eliminate both the neural and behavioral correlates of tinnitus in rats (Nature, 2011). Encouraging early results in tinnitus patients suggest that VNS-directed neural plasticity might be useful for treating other common neurological disorders, including amblyopia, stroke, dyslexia, and autism. Restoring normal function is likely to require a detailed understanding of the mechanisms relating neural activity to behavior. Similarities in animal and human speech sound processing suggest that it will be possible to conduct extensive preclinical testing of novel human therapies for communication disorders.

Roles of attention and reward in perceptual learning. Takeo Watanabe and Yuka Sasaki, Boston University - Perceptual learning (PL) is defined as long-term performance improvement on a perceptual task as a result of perceptual experience. We first found that PL occurs for task-irrelevant and subthreshold features and that pairing task-irrelevant features with rewards is key to task-irrelevant PL (TIPL). These results suggest that PL occurs as a result of interactions between reinforcement and bottom-up stimulus signals. On the other hand, fMRI study results indicate that lateral prefrontal cortex fails to detect and thus to suppress subthreshold task-irrelevant signals. This leads to the paradoxical effect that a signal that is below, but close to, one's discrimination threshold ends up being stronger than suprathreshold signals. We confirmed this mechanism by showing that task-irrelevant learning occurs only when a presented feature is under and close to the threshold. From all of these results, we conclude that attention and reward play different roles in PL.

Perceptual learning and cognition. Merav Ahissar, The Hebrew University of Jerusalem - Perceptual learning was traditionally viewed as different from cognitive learning. Whereas the first focused on its effects on earlier processing stages, showing its specificity to the trained inputs, the latter focused on conceptual plasticity and generalization. I now propose that in both, the crux of learning involves the formation of global schemes that capture the structure of task relevant information, based on detecting stimulus regularities. The initially formed schemes are crude, and they are gradually refined with further practice. This general characteristic applies to simple discriminations as well as to learning of syntax and story comprehension. I will show the dynamics and specificity of this scheme formation for the case of simple 2-tone frequency discrimination. Although the task requires fine discriminations, performance is very sensitive to the structure of cross trial stimulus regularities, and learning is specific to this structure. I will discuss the impact of this "scheme based" conceptualization on the expected impact of different training protocols.

Monday, September 19, 11:00 am – 12:30 pm

Panel Discussion: Translating Neuroscience into Marketable Therapeutic Interventions

Part 1: From Research Findings to Business Plan

Chair: George Rose

Speakers:


Uri Polat


Adam Haim


Laird Malamed


Dan Dardani


Henry Mahncke


Alice Medalia

Alvaro Fernandez

Jessica Lindl

BIOGRAPHIES

Taking a clinically proven treatment and developing a commercial product. Uri Polat, Ucansi Inc. and Tel-Aviv University - Dr. Polat is the director of the Visual and Clinical Neuroscience Laboratory at the Eye Research Institute at the Sheba Medical Center, Faculty of Medicine, Tel-Aviv University. He received a PhD in Brain Research from the Weizmann institute of Science, Rehovot, Israel. He was at the Smith-Kettlewell Eye Research Institute, San-Francisco, USA for several years as a Fellow and Associate Scientist.

In addition to his academic carrier, Dr. Polat developed a successful entrepreneurial carrier and is personally responsible for two groundbreaking business ventures; as the co-Founder and Chief Scientific Officer of Ucansi Inc. and, previously, as the Founder and Chief Scientific Officer of NeuroVision Inc., which developed the first FDA-approved treatment of adult amblyopia.

Ucansi Inc. is a U.S. corporation with an R&D facility in Israel. The company employs professionals of complementary expertise, including neuroscience, optometry, software development and marketing. Nowadays, the company is launching its GlassesOff® product - a patented non-invasive solution for treating Presbyopia ("aging eye", www.glassesoff.com).

NIMH The Small Business Innovation Research (SBIR) Program — NIH funding for academia-industry partnerships. Adam Haim, Division of Services and Intervention Research (DSIR) - Dr. Adam Haim is the Acting Chief of the Clinical Trials and Biostatistics Branch and the Chief of the Small Business Innovation Research and the Small Business Technology Transfer program for Division of Services and Intervention Research at the National Institute of Mental Health. In his current role, Dr. Haim provides operational oversight, coordination and technical assistance to a broad range of ongoing, national, multi-site clinical studies and manages a portfolio of grants and contracts focused on the development, evaluation and implementation of technology enhanced mental health interventions. Dr. Haim is a licensed clinical psychologist and earned his doctoral degree in clinical psychology from State University of New York at Albany and completed his research fellowship at the NIMH Intramural Program in the Division of Clinical Neuroendocrinology.

Game development. Laird Malamed, Activision - Laird Malamed (Sr. Vice President, Head of Development) oversees software production and hardware development for video game publisher Activision. He helped create the Call of Duty franchise and has held a variety of roles at in his 16+ years tenure. Previously, Malamed worked as a Sound Editor at Sony Pictures and at LucasFilm. He started his career on the award winning Young Indiana Jones Chronicles. Malamed and his wife Dr. Rebecca Rotenberg own Creative Learning Technologies which consults on medical and education projects. CLTC organized the first multi-disciplinary conferences on upper extremity disorders and helped start the American Pain Foundation. It publishes the health blog, www.drrebecca.com. Malamed earned a joint Bachelor of Science degree from MIT in 1989 by crafting his own major of Aeronautical & Astronautical Engineering and Film & Media Studies. He attended USC's graduate cinema program where he is now a part-time instructor. He serves as co-chair of the MIT Club of Southern California's K-12 Learning committee.

Technology transfer. Dan Dardani, MIT - Daniel Dardani is a Technology Licensing Officer at M.I.T.'s Technology Licensing Office. His technology areas include: computer sciences, software, algorithms, digital imaging, video games, and information technologies. Daniel has been with the M.I.T. TLO for 8 years and is well experienced in the scientific, technological, and legal aspects of intellectual property as well as counseling both inventors and entrepreneurs on how to utilize and effectively leverage university technologies into commercialization opportunities. Daniel is a Certified Licensing Professional (CLP) and, in his own time, Daniel helps teach a survey course in Intellectual Property at Harvard University, led by Allan A. Ryan, Director of Intellectual Property for the Harvard Business School Publishing. Before M.I.T., Daniel worked in industry as a senior software test engineer for an international telecommunications and network services company.

Regulatory and reimbursement issues. Henry Mahncke, Posit Science and Brain Plasticity Institute - Dr. Mahncke leads the Research & Outcomes team, designing scientific research and implementing outcomes trials to advance the company's product development. Dr. Mahncke did his graduate work and earned his doctorate in neuroscience in Dr. Merzenich's lab at UCSF. He then worked as an Engagement Manager for McKinsey & Company. While at McKinsey, Dr. Mahncke worked with leading global healthcare and consumer products companies in devising market strategies. Dr. Mahncke has also served in the consulate of the British government as a Science and Technology consultant. He holds a BA from Rice University and a PhD from UCSF

Survey of emerging needs, markets ,and policies. Alvaro Fernandez, SharpBrains Market Research - Alvaro Fernandez is SharpBrains' co-founder and Chief Executive Officer. He has been quoted by The New York Times, Wall Street Journal, CNN, Reuters, and Associated Press, among others. Alvaro is a member of the Global Agenda Councils initiative run by the World Economic Forum, and recently wrote the acclaimed articles, Preparing Society for the Cognitive Age for Frontiers in Neuroscience, and Why We Need to Retool Use It or Lose It, for the Journal of Active Aging. He started his career at McKinsey & Company and led the launch and turnaround of several publishing and education companies in the US and Europe, including Bertelsmann On Line, Docent, Inc, and Edusoft, a unit of Houghton Mifflin. Alvaro has an MBA and MA in Education from Stanford University, and enjoys teaching The Science of Brain Health at SFSU and UC-Berkeley Osher Lifelong Learning Institute.

Consumer preferences. Alice Medalia, Columbia University - Alice Medalia, Ph.D. is an international leader in the field of psychiatric rehabilitation, who focuses on the treatment of neuropsychological disorders in psychiatric illness. She developed the widely used NEAR (Neuropsychological & Educational Approach to Remediation) model to help people with mental illness improve their thinking skills in such areas as attention,

memory, processing speed and problem solving. She lectures and consults to agencies worldwide and conducts training workshops for clinicians who want to learn how to provide cognitive remediation to psychiatric patients. Dr Medalia works with policy makers, researchers, clinicians, families and patients to bring awareness about the impact of cognitive dysfunction on recovery. In order to facilitate greater awareness about cognition in the rehabilitation field, she started the largest conference on this topic, Cognitive Remediation in Psychiatry, which takes place the first Friday in June in New York City. Her research focuses on the factors that impact a successful recovery of neuropsychological functions. Dr Medalia's contributions as a Neuropsychologist, Researcher and Advocate of Cognitive Remediation have won her awards from professional and advocacy groups.

Marketing therapeutic interventions for children. Jessica Lindl Scientific Learning, Inc. - Jessica J. Lindl joined Scientific Learning in March 2007. Previously, Ms. Lindl served as vice president of marketing and product management for Riverdeep, a leading developer of educational software. Ms. Lindl held marketing management positions of increasing responsibility at Riverdeep and The Learning Company, which was acquired by Riverdeep, from 2001 through 2006. Prior to her tenure at Riverdeep, Ms. Lindl served as the director of product management for Simplexis, an e-procurement provider for the K-12 market, in 2000 and 2001 and as part of the sales management team for AT&T in San Francisco from 1995 to 1998. Ms. Lindl holds a bachelor's degree in economics and international studies from Miami University in Oxford, Ohio and an MBA from the Haas School of Business at the University of California, Berkeley.

Monday, September 19, 2:00 pm – 5:00 pm

Demonstrating Meaningful Neural Plasticity in Humans

Chair: Adam Gazzaley

Speakers:

Mark D'Esposito

John Jonides

Adam Gazzaley

Molly Wagster

Cameron Carter

ABSTRACTS

Training-induced changes in functional connectivity in frontal cortex. Mark D'Esposito, UC Berkeley - Our research focuses on investigating the neural bases of high-level cognitive processes such as working memory and executive control. These aims are achieved through several different experimental approaches and methodologies. First, we employ a neuroimaging method called functional MRI (fMRI) to identify the neuroanatomical substrates and temporal dynamics of various cognitive processes in normal human subjects. A key focus has been the cognitive functions supported by prefrontal cortex. Second, we have been investigating the role of the dopaminergic system in working memory and frontal lobe function. This aim is achieved with pharmacological studies during which direct dopaminergic agonists are administered to normal human subjects, as well as patients with frontal lobe lesions, to determine the effect of dopamine on cognition. Third, we perform behavioral studies in patient populations with frontal lobe dysfunction (e.g. stroke, head injury, Parkinson's disease) in order to further understand the mechanisms that underlie working memory. Finally, we are interested in understanding the physiological bases of normal human aging, and the effects of normal aging on prefrontal function.

Improving fluid intelligence via cognitive training. John Jonides, University of Michigan - Cognitive training has been shown to transfer to various tasks. Previous research has found an important such transfer effect: Training on short-term memory improves performances on measures of fluid intelligence which are closely related to professional and educational success. Although there is accumulating evidence for this transfer effect, knowledge about the underlying mechanisms is scarce. Here we show that a seven-day training program on working memory leads both to decreased cerebral perfusion during task performance and to increased perfusion when not engaged in the task. Furthermore, we found that the brain regions that demonstrated these increases and decreases substantially overlap. This overlap suggests coherence between the two neural effects of training, and it implies that increased perfusion at rest could lead to improved neural efficiency, which in turn facilitates task processing.

Multimodal imaging of neural plasticity after training. Adam Gazzaley, UCSF - Normal aging is associated with diminished perceptual, attention and memory abilities. To remediate age-related deficits, cognitive training programs, often in the form of video games, are increasingly being developed. However, it is not yet clear if, and by what neural mechanisms, such training ameliorates the effects of cognitive aging. I will describe several completed and ongoing studies in our lab that use neural recordings (EEG) before and after a period of game play by older adults to evaluate the neural effects of such training and how it relates to performance changes.

The NIH ToolBox. Molly Wagster, NIA, NIH - At present, there are many studies that collect information on aspects of neural function; unfortunately, there is little uniformity among the measures used to capture these constructs. Investigators have expressed the need for brief assessment tools that could be used as a form of 'common currency' across diverse study designs and populations. To address this need, the NIH is developing a set of instruments to measure cognitive, motor, emotional and sensory function that would allow assessment in individuals ranging from 3 to 85 years of age. The NIH Toolbox provides investigators with an innovative approach that employs state-of-the-art psychometric research and novel testing methods and that will be responsive to research needs in a variety of settings, particularly large cohort studies and prevention or intervention trials. With an available toolbox of measures, yields from these large and very expensive studies can be maximized by allowing a much larger number of important research questions to be studied, with minimal increment in subject burden and cost. By ensuring that the assessment methods are capable of comparison to existing and completed studies and can incorporate modifications in the future, a truly "economic"

and valuable resource for the research community will result.

Translating tasks from cognitive neuroscience into biomarkers of treatment response : The CNTRICS perspective. Cameron Carter, UC Davis - In order to investigate the impact of interventions on human cognition there is a pressing need for measures of cognitive and neural processing that can establish the effects of training on the specific cognitive and neural systems. Traditional clinical measures, which have desirable psychometric properties, lack cognitive specificity. Cognitive neuroscience has a wide array of specific measures however little is known about their psychometric and neurometric properties. This creates a conundrum for measures with poor psychometric properties undermine the power of pivotal studies. In the context of cognition in schizophrenia we sought solutions through the CNTRICS initiative, funded by the NIMH. Over 7 meetings we identified a developmental path and set of behavioral measures and candidate imaging biomarkers for development as "industrial" measures. Follow-up studies have led the optimization of a subset of these, engaging cognitive control, episodic memory, perceptual integration and visual surround suppression. Brief versions of the tasks have been developed with robust psychometric properties. Optimization of fMRI paradigms is ongoing. Further details and beta versions of the tasks are available at cntrics.ucdavis.edu.

Tuesday, September 20, 8:30 am – 12:00 pm

Neural Plasticity and Cognitive Training in Impaired Individuals across the Lifespan

Chair: Torkel Klingberg

Speakers:

Torkel Klingberg

Yair Bar-Haim

Nina Kraus

Sophia Vinogradov

Karlene Ball

Joshua Cantor

Wayne Gordon

ABSTRACTS

Working memory training in children with attention deficits. Torkel Klingberg, Karolinska Institute - Impaired working memory is associated with low academic performance and with distractability and inattention in clinically defined groups, such as in ADHD, but the same associations are also relevant in the general population. Klingberg and collaborators have developed and tested a computerized method for training working memory. Several studies have shown that working memory can be improved by this method, and that performance improves also on non-trained tasks demanding working memory. Moreover, improving working memory also decreases the symptoms of inattention in everyday life. This has now been confirmed by several, independent research groups. Klingberg and collegues has also shown that training of working memory changes brain activity in frontal and parietal regions, and is associated with changes in the density of dopamine D1-receptors in the cortex. Training of working memory might thus be a non-pharmacological way to address the key cognitive function in children with low working memory. Future question concern which other cognitive functions that can be trained, and how strong transfer is between functions.

Computerized training for anxiety disorders in children. Yair Bar-Haim, Tel Aviv University - Attention Bias Modification (ABM) is an immerging therapy for anxiety disorders rooted in current neurocognitive models of anxiety and in established experimental data on threat-related attentional biases in anxiety. ABM treatments utilize computer-based training to implicitly modify biased attentional patterns. The extant evidence of ABM efficacy and its relation to neural plasticity will be reviewed. Novel evidence indicating that ABM may become an efficacious treatment for anxious children will be described in three studies: Study 1 establishes that ABM may be applied in children and that threat-related attentional bias causally affects stress vulnerability; Study 2 indicates that ABM designed to facilitate disengagement of attention from threats reduces stress vulnerability in high-anxious children; Study 3 describes the efficacy of ABM treatment in a randomized controlled trial with clinically anxious children. Gaps in need of bridging before ABM could be routinely applied in standard treatment protocols for pediatric anxiety will be outlined.

Music and software-based training for the development and maintenance of communication skills. Nina Kraus, Northwestern University - Music and software-based training for the development and maintenance of communication skills. How do you make a better learner? Auditory-based communication skills are developed at a young age and are maintained throughout our lives. However, some individuals, both young and old, encounter difficulties in achieving or maintaining communication proficiency. I am interested in the biology of learning in humans, in particular at the intersection of hearing and cognition. Our comprehensive approach has revealed that biological signals arising from hearing sounds relate to real-life communication skills such as listening to speech in noisy environments and reading. Experience and computer-based training can improve these biological signals. In this talk, I present some findings of biological plasticity following musical experience and software-based training in a variety of subject populations, relate them to attention and auditory memory, and present a model that summarizes the reciprocal influence of sensation and cognition on neural processing.

Computerized cognitive training in schizophrenia. Sophia Vinogradov, UCSF - Schizophrenia is a chronic debilitating psychiatric illness characterized by impaired cognition. To date, no available treatments are effective for the cognitive dysfunction, which has a profound impact on patients' community functioning and quality of life. We report longitudinal behavioral, biomarker, MEG, and fMRI data from clinically stable adult outpatients with schizophrenia who were randomly assigned to participate either in 50 hours of "neuroplasticity-based" computerized cognitive training or 50 hours of a computer games control condition. Participants engaged in a heavy schedule of computerized training that focused on auditory perception and accurate speech reception; the psychophysical training was embedded within increasingly complex auditory and verbal working memory/verbal learning exercises. The goal was to increase the accuracy,

the temporally-detailed resolution, and the power of auditory inputs feeding verbal memory processes.

Subjects in the active training condition, but not the control group, show: 1) Significant improvements in neurocognitive outcome measures that are correlated with improved quality of life 6 months later; 2) Significant increases in serum BDNF and d-serine levels; 3) MEG data indicating improved efficiency in early auditory processing and in prefrontal activation, as well as changes in resting state functional connectivity; 4) fMRI data showing more normal brain activation patterns during verbal memory tasks. Taken together, these data indicate that 50 hours of neuroplasticity-based cognitive training drives behavioral and neurobiological changes consistent with enhancement and restoration of key neurocognitive processes in the brain.

Cognitive training for Traumatic Brain Injury. Wayne Gordon and Joshua Cantor, Mount Sinai School of Medicine - Computer based-interventions that take advantage of neuroplasticity may be of benefit to individuals with traumatic brain injury (TBI) acutely or long after injury. Data are presented from two studies on the feasibility of using a computerized brain plasticity-based cognitive training (BPCT) program for individuals with TBI a) on an inpatient rehabilitation unit and b) dwelling in the community. The studies demonstrated that inpatients with significant impairment were able to use the program on a laptop computer and reported that the experience was positive. Barriers to inpatient use were identified. The community-based individuals (n=10) were able to use the software independently in their homes. Participants reported subjective improvement in cognitive functioning and improvements on neuropsychological measures were noted. BPCT may be a viable intervention for individuals with TBI as a component of comprehensive neurorehabilitation. Further studies are warranted.

Age-related cognitive decline, cognitive training, and transfer to everyday performance. Karlene Ball, University of Alabama at Birmingham - Processing speed is one of the first cognitive abilities to decline with age and is a key function to maintaining independence. Fortunately, it is possible to reverse or maintain this ability through a targeted 10 hours of a computerized cognitive training program. Research from two multi-site randomized clinical trials have demonstrated maintained improvements in processing speed and translation to a variety of mobility, health and wellbeing outcomes. Older adults who completed this training have demonstrated maintained processing speed, maintained driving mobility, a 50% reduction in at-fault crashes, maintained health (via reduced heath expenditures and maintained self-rated health), reduced risk for clinically-relevant depression, and maintained health-related quality of life. The effects are maintained across a three-to-five year period. Such effects are increased with booster training (4-8 hours). Considering the importance of these outcomes, these interventions have great potential to sustain independence and quality of life of older adults.

Tuesday, September 20, 12:30 pm – 1:45 pm

Panel Discussion: Translating Neuroscience into Marketable Therapeutic Interventions Part 2: From Product to Consumer

Chair: George Rose

Panelists:

Uri Polat

Adam Haim

Laird Malamed

Dan Dardani

Henry Mahncke

Alice Medalia

Alvaro Fernandez **Jessica Lindl**

BIOGRAPHIES – (see above Part 1)

Tuesday, September 20, 2:00 pm – 5:30 pm

Future Directions and Future Innovations

Chair: Daphne Bavelier

Speakers:

Daphne Bavelier

Alvaro Pascual-Leone

Jim Blascovich

Michael Merzenich

Paula Tallal

Alan Gershenfeld

ABSTRACTS

How can we promote learning to learn? Action video games as exemplary learning tools. Daphne Bavelier, University of Rochester - Technology, from chatting on the internet to playing video games, has invaded all aspects of our lives and, for better or for worse, is changing who we are. Can we harness technology to effect more changes for the better? Yes we can, and not always in the way one might have expected. In a surprising twist, a mind-numbing activity such as playing action video games appears to lead to

a variety of behavioral enhancements in young adults. Action video game players outperform their non-action-game playing peers on various sensory, attentional and cognitive tasks. They search for a target in a cluttered environment more efficiently, are able to track more objects at once, process rapidly fleeting images more accurately and switch between tasks more flexibly. In addition, action gamers manifest a large decrease in reaction time as compared to their non-action-game playing peers across many different tasks, without paying a price in accuracy. A training regimen whose benefits are so broad is unprecedented and provides a unique opportunity to identify factors that underlie generalization of learning and principles of brain plasticity. We propose that a common mechanism is at the source of this wide range of skill improvement. In particular, improvement in performance following action video game play may result from greater attentional control with gamers focusing on signal and ignoring distraction more efficiently. This in turn allows for enhanced integration of information during decision making with action gamers making more informed decision about their environment. We show how these processes may be be implemented by more faithful Bayesian inferences within neural networks consistent with the view that action gamers learn to learn.

How can we combine brain stimulation techniques with cognitive training? Alvaro Pascual-Leone, MD, PhD, Berenson-Allen Center for Noninvasive Brain Stimulation, Beth Israel Deaconess Medical Center and Harvard Medical School, Boston, MA - Brain stimulation techniques enable modulation of activity in targeted brain regions and distributed brain networks. While mechanisms of action remain uncertain, there is evidence supporting the notion of neuromodulation involves in part changes in connectivity and induction of synaptic plastic changes. Such effects, might be leveraged to potentiate the effects of behavioral and cognitive training. Noninvasive brain stimulation techniques, such as transcranial magnetic stimulation (TMS) and transcranial direct current stimulation (tDCS), are particularly appealing in this regard. Proof of principle studies support the notion that it is possible to enhance the effects of cognitive and behavioral training by TMS or tDCS applied at specific parameters, targeting specific brain regions, and delivered at specific times in relation to the training. Brain stimulation may be a valuable adjunct to increase the efficacy of behavioral and cognitive training.

How Does immersive VR influence brain motivational systems? Jim Blascovich, University of California Santa Barbara - This presentation describes biopsychosocial model of challenge and threat motivation and applicable research based on neuroendocrine-based data as a rationale to explain and better understand subtle iatrogenic treatment effects that can unintentionally limit the efficacy of intensive pharmacological and radiological treatments. A rationale for ameliorating such effects using modern digital virtual reality technology is delineated. Relevant data from past research involving membership in stigmatized groups that bolster the iatrogenic argument are reviewed as are data from exploratory research relevant to amelioration.

Is There Any Limit to the Disorders That Can Respond to Computerized Training? Michael Merzenich, Brain Plasticity Institute, Posit Science Corporation, San Francisco - Neuroscience studies conducted primarily over the past three decades have now broadly defined the fundamental neurological processes that account for the acquisition and improvement of skills and abilities across the human lifetime. An equally large body of studies have documented the distortions in the physical and functional brain – as well as the parallel behavioral disabilities – that define a rich variety of neurological and psychiatric conditions that degrade human lives. These two scientific domains provide us with an increasingly intelligent basis for considering how brain plasticity- guided computer training might be deployed to drive neurobehavioral 'corrections' that can be expected to result in a) the prevention of, b) the amelioration of, or c) the possible recovery from many neurologically-based conditions. Using aging infirmity, recovery from stroke and schizophrenia patient training examples, I shall briefly review the state of progress and the promise for – as well as some of the inherent limitations that shall impact the immediate reach of -- this new form of neuroscience-based 'medicine'.

Making cognitive training effective, addictive and viral: What can scientists and the gaming industry learn from each other? Paula Tallal, Rutgers - After focusing on basic neurocognitive research on language development and disorders for 20 years, in 1993 my laboratory embarked on determining if this body of research might have practical implications for intervention. In collaboration with the Merzenich lab, we developed a series of neural training exercises, disguised as video games, to determine if "neuroplasticity-based training" could improve learning in children. The results of controlled, laboratory studies demonstrated, for the first time, that basic perceptual, cognitive and linguistic skills were highly plastic and could be significantly improved through neuroplasticity-based training. We subsequently have focused on how to use computer gaming and Internet technologies to translate basic research out of the laboratory, for anytime, anywhere use, while still maintaining efficacy. While scientists understand how to make games effective in driving beneficial neural change, the gaming industry understands how to maintain attention and compliance needed for efficacy- making games that are addictive and viral.

What will be the social impact of harnessing games for brain health? Alan Gershenfeld, E-Line Media - In this talk, Alan Gershenfeld will provide a high-level overview of trends in the growing impact game sector and methodologies for designing, developing and publishing games that seek to make meaningful learning, health and social impact. He will also explore specific examples of how research-based brain games can move from academic research to 'impact-friendly' commercial products and services with aligned research, design, commercial and impact goals.

Mr. Gershenfeld has spent the last twenty-five years at the intersection of entertainment, technology, and social entrepreneurship. He is currently Founder and President of E-Line Media, a publisher of digital entertainment that engages and empowers – with a core focus on computer/video games and webcomics.

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Visual Learning

#1

Perceptual learning transfers to untrained retinal locations after double training: A piggybacking effect. Rui Wang[1], Jun-Yun Zhang[1], Stan Klein[2], Dennis Levi[2], Cong Yu[1]; [1]Beijing Normal University, [2]UC Berkeley - Perceptual learning (PL) can transfer to a new retinal location if additional training with an irrelevant task primes the new location, suggesting PL a more general learning process occurring in non-retinotopic high brain areas. This double training for the first time allows us to study the true facets of PL transfer.

We measured the transfer of Vernier learning, which is typically location specific, to completely untrained locations after double-training. (1) Vernier learning transferred to completely untrained locations if two orthogonal Vernier stimuli were trained at separate visual quadrants, but not if trained at the same location. (2) When Vernier and a new task were trained at diagonal quadrants, respectively, Vernier learning always transferred to the diagonal quadrant. However, whether it also transferred to other completely untrained quadrants depended on the location specificity of the new task. Location-non-specific motion direction or orientation learning can piggyback Vernier learning to other locations, but location-specific contrast learning cannot. (3) Similar piggybacking was observed when Vernier and a new task were trained at the same location. (4) The main results of the above were replicated in the transfer of contrast and texture discrimination learning.

These results indicate that the brain can learn to discount the location information and make PL solely feature-based when a same task is trained at two locations. For motion/orientation learning the learned decision unit may always connect to other locations because motion/orientation stimuli are globally connected. Location specific learning can be piggybacked to other retinal locations through these tasks' active network.

#2

Learning To Decide Faster: More Hits For Higher Speed. Oren Yehezkel[1], Anna Sterkin[1], Uri Polat[1]; [1]Goldschleger Eye Research Institute, Sheba Medical Center, Tel Hashomer 52621, Israel - Our recent findings provided a neurophysiological marker for collinear contrast facilitation in detecting low-contrast Gabor patches (GPs) (negative ERP N1-peak amplitude, at 260-msec). These collinear interactions, in behavior and ERPs, were abolished by suppression induced by backward masking (BM), suggesting that suppression induced by BM eliminates collinear facilitation (Sterkin, Yehezkel, Bonneh, Norcia and Polat, 2008; 2009). Moreover, training on BM task overcomes BM, improving processing speed (Polat 2009). Here we trained target-detection followed by BM to study whether reinforced facilitatory interactions can overcome BM. ERPs were recorded before and after ten training sessions performed on different days. Low-contrast, foveal target GP with collinear high-contrast flankers were followed by identical flankers (BM) at different time-intervals (ISIs). Before training, BM induced suppression of target-detection, at ISI of 50-msec. After training, behavior remarkably improved, including percent correct, sensitivity (d'), reaction time (RT) and decision criterion. For ERPs, before training, BM canceled the physiological markers of facilitation at ISI of 50-msec (N1-peak amplitude). After training, sensory representation (P1-peak) has not changed, however shorter latency (by 20-msec, at 240-msec) and increased N1-amplitude represent development of faster and stronger facilitatory lateral interactions between target and flankers. Thus, previously effective BM became ineffective in disrupting collinear facilitation. Moreover, a high-amplitude late peak (P4, at 610-630-msec), possibly reflecting executive function, was not affected by training, however its high correlation with RT (95%) before training was significantly decreased (76%), consistent with lower-level representation of trained skills. We suggest that perceptual learning strengthening collinear facilitation results in faster processing speed.

#3

Modified Unreal Tournament: An action game therapy for Amblyopia. Indu Vedamurthy[1], Mor Nahum[2], Jessica D. Bayliss[3], Daphne Bavelier[1], Dennis M. Levi[2]; 1University of Rochester, [2]University of California at Berkeley, [3]Rochester Institute of Technology - A novel, non-invasive tool has been developed by customizing a popular first-person action video game, Unreal Tournament (UT) 2004, for the treatment of amblyopia. Amblyopia is a developmental disorder characterized by reduced visual acuity and other higher-order vision deficits. In addition, during binocular viewing, signals from the fellow eye inhibit the amblyopic eye preventing proper co-ordination between the two eyes and compromising stereovision. Our UT custom-game offers a principled method to determine whether binocular training would be beneficial to restoring vision in the amblyopic eye and binocularity. Five major game adaptations were implemented in order to achieve these goals. First, split screen images of the game were presented to each eye through a stereoscope. Second, the image contrast to the fellow eye was degraded, so that the amblyopic eye was placed at a competitive advantage. Third, suppression checks were included to ensure that the amblyopic eye was functioning during dichoptic viewing. Fourth, easier game levels were created to help game-naÃ¯ve participants to learn how to play the game. Fifth, an orientation-discrimination task using Gabor patches was embedded in the game play, targeting only the amblyopic eye to increase the "workload" of that eye during binocular game play. Correct responses were reinforced with game rewards, and incorrect responses were punished by spawning new enemies. The custom-game was piloted on optically blurred non-amblyopic subjects to mimic the situation of amblyopic patients. We conclude that this new adapted UT game platform is engaging and effective, and has promising potential for clinical application.

#4

Non-Invasive neurostimulation on occipital and posterior parietal regions lastingly speeds up detection of foveally presented peri-threshold visual stimuli in the human brain. Antoni Valero-Cabre[1,2,3], Jarrett Rushmore[1], Seth Elkin-Frankston[1]; [1]Laboratory for Cerebral Dynamics, Plasticity & Rehabilitation, Boston University School of Medicine, Boston USA, [2]Université Pierre et Marie Curie, CNRS UMR 7225, INSERM UMRS 975, Institut du Cerveau et la Moelle (ICM), Paris France, [3]Cognitive Neuroscience and Information Technology Research Program, Open University of Catalonia (UOC), Barcelona, Spain - Visual acuity is an essential property of the visual system, which determines our ability to resolve fine spatial detail. It is thought to be highly dependent upon the state of early visual brain areas and the

modulation from posterior parietal sites. In two separate experiments, we examined in human healthy subjects (n=9) the relationship between visual detection and the functional integrity of early visual areas (V1-V4, Experiment 1) or the right posterior parietal regions (IPS, Experiment 2). These two cortical regions were transiently interfered by means of low frequency repetitive Transcranial Magnetic Stimulation (rTMS, 1 Hz, 1200 pulses). Visual acuity was determined before and after rTMS with a paradigm in which subjects acknowledged by the presence of Gabor at 12 cpd and 3 cpd, as appearing in a first (T1) or second (T2) time interval in central vision. We found that V1-V4 rTMS was unable to modulate the contrast sensitivity function (CSF) for any spatial frequency, but induced significant decreases in response reaction times (RT) to low (3 cpd) but not high frequency (12 cpd) peri-threshold Gabor stimuli. The deactivation of the IPS induced similar decreases in RT for both, low and high spatial frequencies. Our data suggest that interfering with early cortical processing either directly, or via feedback projections has the potential to speed-up foveal visual processing. On the basis of the frequency effects, we also hypothesize that, offline suppression of early visual cortex might allow for faster visual processing through the release of inhibition on tectal systems.

#5

Activity-dependent enhancements of conscious vision by non-invasive neurostimulation of the frontal human brain. Antoni Valero-Cabre[1,3,4], Ana Chica[2], Lorena Chanes[1]; [1]CNRS UMR 7225-CRICM, Institut du Cerveau et la Moelle. Paris, France, [2]INSERM UMR S975-CRICM, Institut du Cerveau et la Moelle. Paris, France, [3]Laboratory of Cerebral Dynamics, Plasticity and Rehabilitation, Boston University School of Medicine, Boston, USA, 4Cognitive Neuroscience and Information Technology Research Program, Open University of Catalonia (UOC), Barcelona, Spain - Prior evidence has shown that cue-driven spatial attentional orienting modulate several aspects of visual performance. Similarly, Transcranial Magnetic Stimulation (TMS) on attentional areas has been proved to yield short-lasting visual performance modulations. We explored the effects of TMS on the right Frontal Eye Field (FEF), an attentional orienting relevant area, alone or in conjunction with visuospatial cueing, and gauged its ability to enhance perception of low-contrast near-threshold Gabor stimuli. Two experiments were carried over. In every trial, participants were required, after the presentation of a low-contrast near-threshold Gabor stimulus, to serially perform a forced choice categorization task, consisting of determining the orientation of the Gabor lines (Left or Right?) followed by a detection task (Did you see the stimulus? Where?). In Experiment 1, the Gabor was preceded by a single TMS pulse delivered on the right FEF, whereas in Experiment 2 the Gabor was preceded by both, the cue and the TMS pulse. In Experiment 2, time-locked isolated TMS pulses showed a very mild potential to modulate any of the two tasks. Interestingly, however, the combination of a single TMS pulse delivered on the right FEF with a visuospatial cue in Experiment 3 resulted in significant bilateral enhancements of conscious visual detection, beyond the levels achieved using the visuospatial cue alone. Our results reveal the potential and limitations of time-locked TMS pulses alone or combined with visuo-spatial cueing to punctually boost conscious visual performance, setting up a path for further explorations in visual rehabilitation.

Auditory and Verbal Learning

#6

Accurate Auditory Reproduction Improves Observational Learning Speed and Retention. Jared Cooney Horvath[1], Zach Gray[1], Ilya Vidrin[1], Lukas Schilberg[1], Alvaro Pascual-Leone[1]; [1]The Berenson Allen Center for Noninvasive Brain Stimulation, Beth Israel Deaconess Medical Center, Harvard Medical School - Observational learning "the reproduction of a novel skill following the visual observation of said skill" has long been a mainstay of technology-based educational practice. Utilizing two studies, we examined the effects of varied auditory feedback patterns on observational motor learning and retention. In the first study, participants alternated between watching a silent video of a musician playing a piano sequence (the sound of the piano was removed) and reproducing the piano-sequence themselves. During reproduction, some subjects heard no piano sound, some heard an accurate piano sound, some heard a constant but non-sequential piano sound, and some heard randomly generated piano sounds. It was found that participants who heard no sound during reproduction learned the sequence significantly faster and retained the sequence better over the course of three consecutive days. In the second study, participants alternated between watching a full-audio video of a musician playing a piano sequence (the sound of the piano was included) and reproducing the piano-sequence themselves. During reproduction, some subjects heard an accurate piano sound whilst some heard no piano sound. It was found that participants who heard the accurate piano sound during reproduction learned the sequence significantly faster and retained the sequence better over the course of two consecutive days. We conclude that, during observational learning, accurate auditory reproduction of the observed behavior leads to faster learning and better retention "regardless of the original auditory characteristics. This finding holds important implications for computer/console based observational learning programs and online classrooms.

#7

Auditory frequency discrimination: ERP markers for separate mechanisms underlying individual differences among Dyslexics and controls. Sagi Jaffe[1], Yamit Cohen[1], Merav Ahissar[1]; [1]Hebrew University of Jerusalem, Israel, - Dyslexic participants perform poorer than controls in auditory frequency discrimination, particularly when there is a repeated learnable structure in the stimuli sequence (Ahissar, et al., 2006). We now ask whether there are differences in the ERPs elicited during passive presentation of these stimuli. Average ERP responses of the two groups are very similar, despite controls' better performance. Yet, ERP responses, specifically the mid-latency components N1 and P2, induced even in passive listening, are correlated with performance within both groups. Among controls, but not among dyslexics, P2 was elicited with a larger delay among poor performing participants. Among Dyslexics, but not among controls, poor performers had smaller N1-P2 peak-to-peak amplitude. This double dissociation suggests that the mechanism underlying poor performance differs between groups. Since performance in this task is correlated with various reading and phonological skills in both groups, these observations suggest different sources of difficulties in general, automatic mechanisms of auditory regularity detection.

#8

Supra-modal benefit of Tetris plus auditory training. Yu-Xuan Zhang1, Sygal Amitay1, David R. Moore1; 1MRC Institute of Hearing Research, UK - We previously reported that single session of Tetris, a popular computer game that requires fast visual-motor control, improved tone frequency discrimination (FD). One explanation is that playing Tetris provides supra-modal arousal that facilitates contextual or procedural learning, which would saturate quickly and afford little practical benefit. Alternatively, as action games have been shown to improve visual attention, playing

Tetris may improve some cognitive processes, which would continue with further training and may add to FD training effect. To test these hypotheses, we trained three participant groups for four successive daily sessions, either on Tetris alone, FD with a roving standard (FDr), or Tetris alternating with FDr (FDr+Tetris). Before and after training, all participants were tested on FD with roving and fixed standards, auditory working memory for frequency (WMf), and the visual Attention Network Test (ANT). The Tetris group improved on all of the FD conditions, but by the same amount as an untrained Control group. Neither the Tetris nor the Control group improved on WMf or ANT. Thus, training Tetris alone does not produce perceptual or cognitive benefit beyond the test-retest effect. Both FDr groups showed greater FDr improvement than controls. Interestingly, the FDr+Tetris group improved more and faster than the FDr group. Thus, although Tetris playing alone showed little long-term benefit, it enhanced learning when intermixed with auditory training. Moreover, both FDr learning and its enhancement by Tetris transferred to WMf but not to ANT, suggesting that the training effect is mediated by working memory more than attention.

#9

Less pain more gain: Enhancing learning on perceptual and speech tasks by combining practice with periods of additional sensory stimulation. Beverly A. Wright[1], Nicole Marrone[1], Melissa Baese-Berk[1], Ann R. Bradlow[1]; [1]Northwestern University - Perceptual skills improve with practice, providing a method to treat sensory deficits or to enhance normal perceptual abilities. However, improvement on most perceptual tasks requires considerable time and effort, because mere exposure to sensory stimuli rarely yields learning. We recently reported that this effort can be reduced dramatically simply by alternating performance of the task to be learned with stimulus exposure alone [Wright et al., 2010. J. Neuro. 30, 12868-12877]. In that investigation the task was to distinguish between two tones with similar frequencies. Here we show that the effectiveness of this training technique extends to the categorization of non-native phonetic contrasts and adaptation to foreign-accented speech. In separate experiments, native, monolingual English speakers were trained either to categorize a Thai phonetic contrast or to transcribe sentences spoken in English by non-native speakers. For both speech tasks, alternation between periods of performing the target task and periods of additional exposures to the same stimuli while performing a written task yielded more learning than did the same amount of target-task performance, but with no additional exposures during the written task. Thus, the additional stimulus exposures enhanced learning. The task+exposure regimen also yielded more learning than did stimulus exposure alone, and at least as much learning as did performing the target task for the entire training period. The robust effectiveness of this new training regimen indicates that by properly utilizing additional stimulation one may reduce the amount of practice needed and markedly improve the efficiency of perceptual training schemes. [Supported by NIH/NIDCD.]

Working Memory, Attention, Executive Functions

#10

Model Successfully Predicts Relative Degree of Transfer of Cognitive Training Under Natural Use Conditions for a Web-Based Training Program. Tieming Ji1[2], Joseph L Hardy[2], Benjamin Katz[2], Michael Scanlon[2]; [1]Iowa State University, [2]Lumos Labs - Transfer of benefits from trained exercises to untrained cognitive abilities is a fundamental issue in cognitive training research. Currently, a comprehensive framework linking particular training exercises to specific transfer benefits is lacking. We present a model that predicts transfer of cognitive training benefits based on empirically defined shared underlying cognitive mechanisms. We used this model to successfully predict the relative amount of far transfer from intra-domain and extra-domain exercises to a well-known neuropsychological assessment (Trail Making Test, part B) in a large data set under natural use conditions. Dimension reduction techniques (principal components) and cluster analyses were used to define the membership of each of the 36 training exercises on the website Lumosity.com and the assessment Trail Making B into one of 5 empirically defined cognitive domains (n=1087, ages 15-75). A generalized linear model (GLM) was constructed to test the independent effects of transfer of cognitive training either within the same domain as the assessment or outside the domain (independent sample from initial analysis, n=1439, ages 15-75). Fitted transfer coefficients were significant both for the intra-domain exercises and extra-domain exercises, indicating both far and very far transfer. However, as predicted, the degree of transfer from exercises within the same empirically defined domain was substantially greater than that from exercises outside the domain. Thus, we simultaneously demonstrate a model for predicting the relative degree of cognitive training transfer and the efficacy of an online cognitive training program under natural use conditions.

#11

Neural organization and intra-individual variation in working memory capacity. Alexander Stevens[1], Sarah Tappon[1], Damien Fair[1]; [1]Oregon Health & Science University - Attempts to enhance cognitive function using techniques such as working memory training have met with mixed success. While training techniques may be successful in specific improvements on the trained cognitive tasks, generalization is rarely achieved. Cognitive performance varies from day to day, presumably reflecting both stable and dynamic properties of neural organization. Working memory, a core cognitive function, is likely sensitive to the organizational state of neural networks underlying complex cognitive functions. We tested individuals' working memory capacity and acquired their resting-state fMRI data on two different days. Network modularity, a graph-theoretic measure of network organization, predicted individual differences in memory capacity as well as its intra-individual variation across the two sessions. Moreover, the variability in working memory accounted for by network analysis was largely independent of the stable component of working memory performance. This suggests that the functional organization of the overall network, even in the absence of imposed tasks, influences the expression of working memory capacity even though the actual memory representations may well be focal. The modularity in this network may thus be capturing the confluence of systemic, psychological, and environmental factors that influence its large-scale neural organization, and which in turn affects the actual expression of latent cognitive capabilities. Additionally, it provides insight into a potential source of variability in cognitive performance that is otherwise confounded with task performance. Thus, resting state fMRI may provide new insights into the influence of training on neural systems as well as sources of variation in cognitive learning and performance.

#12

Intensive reasoning training alters patterns of brain connectivity at rest. Allyson P. Mackey[1], Alison T. Miller-Singley[2], Silvia A. Bunge[2]; [1]Helen Wills Neuroscience, UC Berkeley, [2]Department of Psychology, UC Berkeley - Correlations in BOLD activity at rest have been shown to reflect a number of functionally relevant networks, including a fronto-parietal network. While networks detected at rest have often been interpreted to be stable traits, changes in these networks may reflect activity-dependent neuroplasticity. Neuroimaging studies have consistently demonstrated the involvement

of a fronto-parietal network in reasoning ability. Rostrolateral prefrontal cortex (RLPFC), specifically, has been implicated in relational reasoning, or the ability to jointly consider multiple mental representations. We hypothesized that intensive relational reasoning training would lead to repeated co-activation of RLPFC and other frontoparietal regions, altering the connectivity of this network. Rather than designing an artificial training program, we chose to study individuals while they prepared for a standardized test that taxes reasoning ability, the Law School Admissions Test (LSAT). We recruited students who were taking an LSAT course that offers 70 hours of reasoning instruction (n=25), as well as age- and IQ-matched pre-law controls (n=24). Resting-state data was collected for all subjects during two scanning sessions 90 days apart. In the LSAT group, but not in the control group, we found a training-related increase in connectivity between left RLPFC and right posterior parietal cortex, and a decrease in connectivity between left RLPFC and left lateral frontal regions. No significant changes in resting-state connectivity for right RLPFC were observed in either group. These findings provide the first evidence that relational reasoning training can alter resting-state connectivity in the predominantly left-hemisphere network that supports this high-level cognitive capacity.

#13

Sequence-specific and non-specific gains in working memory following cognitive training. Kathryn Gigler[1], Paul Reber[1]; [1]Northwestern University - Working memory (WM) refers to the ability to hold a limited amount of information in mind for a short period of time and is a core cognitive component important for many higher-level cognitive functions, including problem solving and language comprehension. A large volume of research indicates that individual WM capacity can be enhanced through training, potentially improving cognitive performance in a variety of domains; however, a major challenge to realizing the value of this approach lies in the tendency of WM gains to be domain-specific, limited to only trained material. The current research utilized a novel visuo-spatial WM training task based on a game-like sequence learning task. It is comprised of two phases wherein a sequence of moving visual cues is first observed and then replicated following a 2-second delay, during which the sequence must be held in WM. Training was adaptive in that the length of the sequences increased as participants improved, increasing demands on WM and maintaining a challenging and engaging level of difficulty. Participants completed 450 trials of training over 2 hour-long sessions across 2 days, with a repeating sequence of spatial locations covertly embedded in 20% of trials. Increased WM capacity was found after training for both repeating and novel sequences, although observed gains were larger for the repeating sequence. The sequence-specific improvements reflect hyper-specific gains in WM capacity following training, while the task-general gains indicate the potential for improving more general WM function through cognitive training utilizing this task.

#14

Changes in search rate but not in the dynamics of exogenous attention in action video game players. Bjorn Hubert-Wallander[1,2], C. Shawn Green[0], Michael Sugarman[1], Daphne Bavelier[1]; [1]University of Rochester, [2]University of Washington, [3]University of Minnesota - Previous studies have shown enhanced speed of processing during visual attention tasks following habitual action video game play. However, using one of the diagnostic tasks of the efficiency of visual processing, a visual search task, Castel and collaborators (Castel, Pratt, & Drummond, 2005) reported no difference in visual search rate, instead proposing that action gaming may change response time execution rather than the efficiency of visual selective attention per se. Here we used two hard visual search tasks, one measuring reaction time and the other accuracy, to test whether visual search rate may be changed by action video game play. We found greater search throughput in the gamer group than in the non-gamer controls, consistent with increased efficiency in visual selective attention. We then asked how general the change in throughput noted so far in gamers may be by testing whether exogenous attentional cues would lead to a disproportional enhancement in attentional throughput in gamers as compared to non-gamers. Interestingly, exogenous cues were found to enhance throughput equivalently between gamers and non-gamers, suggesting that not all mechanisms known to enhance throughput are similarly enhanced in action video gamers.

#15

Modafinil improves learning of implicit spatial probabilities. Beth A Stankevich[1,2], Joy G Geng[0]; [1]Center for Mind and Brain, [2]UC Davis Department of Neuroscience, [3]UC Davis Department of Psychology - Learning about the underlying spatial probabilities implicit in our environment is necessary for deploying attention and for selecting actions. Previous work has shown that dopamine (DA) and norepinephrine (NE) are involved in both choice behavior and attentional selection (Frank et al., 2009; Aston-Jones & Cohen, 2005). Deficient levels of either catecholamine, can result in the inability to use new incoming information to appropriately allocate attention and make choices, e.g., schizophrenia patients with low PFC DA levels have set-shifting deficits (Ceaser et al., 2008). Modafinil is a drug that increases the release of both DA and NE and is associated with task-related activation increases in the prefrontal cortex (PFC) (Minzenberg et al., 2008) Our goal was to investigate the effects of modafinil on the ability to learn the implicit spatial probabilities that governed target locations in a choice behavior task. Fourteen adults (8 female, 14 right handed, ages 26-41 yrs) were tested in a double-blind manipulation of modafinil (200 mg) and placebo over two sessions. We found that modafinil enhanced learning of the probabilistic distribution of targets, led to perseveration of the learned strategy, and produced long-lasting changes whereby "re-learning" the spatial probabilities of the task was more rapid on the second arm of the experiment compared to subjects administered placebo during the first arm. These findings have implications for pharmacological interventions in patients with deficient catecholamine levels (e.g., schizophrenia) as well as increase our understanding of neurotransmitter systems that bias learning involved in attentional selection and choice behavior.

Emotion and Facial Processing

#16

Neurobehavioral intervention for emotion regulation and well-being. Anett Gyurak[1,2,3], James Gross[1], Amit Etkin[0]; [1]Stanford University, Department of Psychology, [2]Stanford University School of Medicine, Department of Psychiatry and Behavioral Sciences, [3]Sierra-Pacific Mental Illness, Research, Education, and Clinical Center (MIRECC) Veterans Affairs Palo Alto Health Care System, Palo Alto, CA - Emerging research suggests that targeted skill training in executive functions (EF) and emotion regulation (ER) may result in neural reorganization of frontal regulation-related brain areas, and enhanced ability to regulate limbic regions involved in emotional reactivity. We sought to evaluate the effectiveness of a web-based neurobehavioral intervention program that targets EF and ER. Participants in Study 1 were healthy young adults and in Study 2 patients with current comorbid Generalized Anxiety Disorder/Major Depressive Disorder (GAD/MDD). Participants in Study 1 completed a 30-day neurobehavioral intervention

program that targeted three aspects of EF (interference, switching, focus) and in Study 2 EF training was combined with an ER-training protocol (reducing negativity and increasing positivity bias).

Results showed that participants in Study 1 experienced improvements in emotion and mood regulation (reduction in anxiety, depression, and increases in beneficial forms of emotion regulation) as compared to control group. Furthermore, improvements in emotion and mood regulation were related to participants' baseline neuroticism, such that those with the greatest neuroticism benefited most from the intervention a " suggesting that patients with GAD/MDD might experience benefits as a result of EF training. Consistent with this reasoning, training of GAD/MDD patients in Study 2 with the combined EF-ER resulted in a decrease in anxiety and depression scores, and increases in beneficial forms of emotion regulation by self-report, as well as improved ER performance on laboratory performance tasks. Collectively these results show evidence for cognitive training in improving emotion regulation and alleviating symptoms in patients with mood and anxiety disorders.

#17

Same-Race Configural Face Training Enhances Face Processing Across Races. Rogelio Mercado[1,2], Sarah Cohan[2], Joseph DeGutis[0]; [1]VA Boston Healthcare System, [2]Harvard University - Few studies have demonstrated training-related face processing improvements in healthy participants. Such training may reduce the other-race effect, same-race (SR) faces being better remembered than other-race (OR) faces, and improve general identity recognition, which may be important for various security professions. Although studies have shown that it is possible to improve OR face memory, few studies have demonstrated improvements in SR face memory. The current study investigated whether configural and holistic face training (training the integration of information from across the entire face into a coherent whole) with SR faces would lead to improvements in processing of both SR and OR faces. Specifically, Caucasian participants performed a 14-day (45 min/day), web-based training program and were assessed pre- and post-training using the Part-Whole Task, a measure of configural and holistic processing, and the Cambridge Face Memory Test. Despite only training on SR faces, participants showed improvements for both SR and OR faces. Specifically, participants improved holistic processing of the eye region for OR faces, noteworthy since the eye region is particularly diagnostic for individuation. Participants also improved their memory of SR and OR faces under degraded viewing conditions. These results suggest that training fostered an automatic bias to attend to configural aspects of all faces and that prior to training, people were not generally at their highest capacity for both SR and OR face processing. These findings show that it is possible to enhance face processing in healthy controls and that these skills can generalize across races.

#18

Online Configural Face Training Promotes a more Normal Pattern of Face Processing in Developmental Prosopagnosics. Sarah Cohan[1], Joseph M. DeGutis[0], Ken Nakayama[1]; [1]Harvard University, [2]VA Boston Healthcare System - Case studies over the last 5 years have shown that it is possible to improve face processing in developmental prosopagnosics (DPs) by training both normal and compensatory mechanisms. However, it is unclear whether these training effects produce real-life improvements and whether these programs can be implemented on a broader scale such as afforded by web-based training. We attempted to address these questions by recruiting a large sample of DPs (N=25) to perform an 3-week online face training program aimed at improving configural and holistic processing (DeGutis 2007). We assessed 4 domains of face/object processing: face perception, memory, part and whole processing, and object perception. The training group also completed a 5-day diary before and after training to quantify potential real-world improvements. Results from the training group were compared to a waitlist control group of DPs. DPs significantly improved their speed and accuracy on the training task. Compared to controls, the training group demonstrated significant improvements on whole trials in the part-whole test, driven by enhanced performance on the eye region. This suggests training promoted a normalized pattern of face processing. Those showing the greatest improvement on the eye region also performed significantly better on several pre-training assessments and the training task, suggesting that these participants may have had a more robust face infrastructure upon enrollment. Unfortunately, group-level test improvements were limited to the part-whole task. In terms of real-world improvements post-training, participants significantly increased their confidence and showed a trend towards reducing their number of face recognition failures.

#19

Screening for Developmental Prosopagnosia (face blindness) in children: developing interventions. Sherryse Corrow[1], Elaine Mahoney[1], Jordan Mathison[1], Elizabeth Greiter[1], Michelle Platt[1], Albert Yonas[1]; [1]University of Minnesota - Children and adults with developmental prosopagnosia (DP) have difficulty recognizing others by their faces despite no known brain injury. This disorder leads to social difficulties for children who cannot recognize friends, teachers, or even their parents. Our goal was to develop measures to examine the course of facial recognition in typically developing children and use these norms to assess children who may be suffering from DP. First, we collected a sample of 249 7, 8, 10, and 13-year-olds and recorded their performance on version of the Cambridge Face Memory Test (CFMT) adapted for children by Pelicano. In this task, children were presented with a face from several angles and asked to identify that face from a series of 2-person line-ups. We found that variance (standard error) was constant across age, and, thus, were able to make a model of the development of typical facial recognition. Then, we tested a 7-year-old subject, B., whose parents identified him as suffering from a severe case of DP. Despite his high intelligence, he scored more than 2 standard deviations below the mean on the CFMT. From these results, we concluded the adapted CFMT may be a valid test for identifying DP children. With entertainment software approaches, we can be more effective in assessing additional children on the internet to further evaluate the validity of our measure. Also, entertainment software graphics could provide DP children with a training program that is interesting enough that they will want to practice sufficiently to improve their facial processing.

Children

#20

Using Neuroplasticity-Based "Video-Games" to Improve Writing Skills. Beth Rogowsky[1,2], Mary Kropiewnicki[2], Rhonda Waskiewicz[2]; [1]Rutgers University, [2]Wilkes University - This randomized control group study investigated the effect of Fast ForWord® neuroplasticity-based "video-games" on 6th grade students' writing skills, specifically their use of content, linguistics, and conventions. Fast ForWord is a series of software training programs (disguised as computer games) which strengthens foundational cognitive skills (memory, attention, processing rate, and sequencing) in the context of phonological awareness, spoken language, and reading comprehension "games". Fast ForWord, based on neuroplasticity research, uses frequent and intense practice, individually adaptive trials, sustained attention,

simultaneous training, and timely rewards to drive neural change. A pretest-posttest experimental design was used. Eighty 6th grade students took the Oral and Written Language Scales (OWLS) Written Expression Scale at the beginning and end of a 45-day marking period. The students were randomly assigned to the Experimental (trained) or waiting list Control group. The Experimental group (N=39) was trained using Fast ForWord Literacy (FFL) and Fast ForWord Reading Level 2 (FFR2) computer software and the Control group (N=41) was not. Both the Control and Experimental groups received the same standards-based language arts curriculum at school. Results from this study showed that the Experimental group made statistically greater improvement (pre- vs. posttest scores) in SEAE (Standard Edited American English) writing skills than the Control group as measured by the OWLS Written Expression Scale ($p < 0.0005$ with an overall effect size between groups of cohen's $d = 0.65$).

#21

Making working memory really work: From the laboratory to schools. Joni Holmes[1], Susan Gathercole[1]; [1]Cognition and Brain Sciences Unit, Cambridge - Working memory (WM) impairments are a common feature in a range of developmental disorders, as well as in the majority of slow learners. Numerous research studies show that Cogmed Working Memory Training (CWMT) leads to substantial WM improvements, with some evidence of improved rates of learning. The aim of this study is to conduct three field trials of CWMT to test its effectiveness under the real conditions in which it will be used in schools. In Trial 1, 50 children aged 9-10 years with the lowest school performance were selected for inclusion. In Trial 2, 45 children aged 12-13 years with the lowest math performance were selected. Both groups completed CWMT in school supervised by school staff only. Comparison groups for both trials were children matched on school performance, gender and age who did not undergo CWMT. In trial 3, 24 mixed ability children aged 7-8 years completed training. Outcome measures were: WM, indexed by improvements on the training tasks for Trials 1 and 2, and by improvements on standardised non-trained WM tasks for Trial 3; scholastic attainment as measured by performance on National assessments; and teacher-based assessments of classroom performance. Gains in WM following training were comparable to those in tightly controlled research studies. There were significant improvements in teacher ratings of classroom performance, with trends towards improvements in scholastic attainment, post-training. Finding that CWMT can effectively boost WM performance under real-world conditions has immense implications for recommendations of best practice for the management of children with WM deficits.

#22

The impact of working memory training on learning: A randomized controlled trial. Darren Dunning[1], Susan Gathercole[2], Joni Holmes[2]; [1]University of York, UK, [2]Cognition and Brain Sciences Unit, Cambridge, 3[4, 5, 6, 7, 8, 9, 10, 11, 12] - Children with poor working memory (WM) typically make slow educational progress due to an inability to meet the heavy WM demands of the classroom. Studies have shown that extensive training on artificial WM tasks benefits performance on other rarefied memory tasks administered under controlled conditions in children and adults. The aim of the current study is to establish whether these benefits will transfer to improvements in children's reading, language and mathematical skills, as well as the practical situations in which WM appears to play a vital role, using a randomised controlled design. Ninety children aged 7-9 years were randomly allocated to one of three conditions: i) active intervention in which children trained on the standard adaptive version of the Cogmed WM training program (CWMT) ii) active control in which children trained on a non-adaptive placebo version of CWMT and iii) passive control in which children received no intervention. All children completed a range of assessments both pre and post training, or before and after 6 weeks of normal schooling. Children in the active intervention group made significantly greater gains in non-trained and practical WM tasks than children in either control group. There were significant post-test differences in reading rate, written expression, processing speed and attention. In all cases gains were significantly greater for the active intervention group. These results demonstrate that training improves WM performance in children with poor WM and may transfer to other skills, including aspects of learning.

#23

The effect of schooling on behavioral and neurological trajectories associated with children's executive functioning skills. Melisa Carrasco[1], Jennie K. Grammer[2], William J. Gehring[2], Frederick J. Morrison[2]; [1]Neurosci. Grad. Program, Univ. of Michigan, ANN ARBOR, MI, [2]Dept. of Psychology, Univ. of Michigan, ANN ARBOR, MI - A growing literature has suggested a direct link between the development of Executing Functions (EF) (e.g., response inhibition, working memory) and children's school success. Relatively no research has been done to describe the electrophysiological correlates of schooling in the development of EF using event-related potentials (ERPs). The purpose of this study was to assess a series of event-related potentials (including the error-related negativity) and to test their relationship to the acquisition of EF skills in young children performing a version of a go-no-go and working memory task. Preliminary findings from an investigation designed to address these questions will be presented. Specifically, pilot behavioral and neurological data collected directly within the elementary school setting from 22 pre-kindergarten, kindergarten, and first grade children will be described. Additionally, efforts to explore schooling effects on brain and behavioral measures of EF using the school-cutoff design will be described and strategies for conducting this work in the school setting will be discussed.

Aging

#24

The Mental Activity and eXercise (MAX) Trial. Deborah Barnes[1,2], Gina Poelke[0], Wendy Santos-Modesitt[0], Arthur Kramer[3], Cynthia Castro[4], Kristine Yaffe[1,2]; 1University of California, San Francisco, [2]San Francisco Veterans Affairs Medical Center, [3]University of Illinois, Champaign-Urbana, [4]Stanford University - Objective: To perform a randomized, controlled trial to compare the effects of different mental and physical activities on cognitive function over 12 weeks in 126 non-demented, inactive older adults with cognitive complaints.

Methods: All study participants were randomized to a mental activity group (Posit Science, San Francisco, CA, or educational DVDs) that performed study-specific computer-based activities at home for 60 minutes/day, 3 days/week, and to an exercise group (aerobic or stretching) that attended study-specific exercise classes at a local YMCA for 60 minutes/day, 3 days/week, for 12 weeks. The primary outcome was global cognitive change using a composite measure from a detailed neuropsychological battery. Analyses were intent-to-treat.

Results: Subjects had a mean age of 73 years; 63% were women and 36% were racial/ethnic minority. There were no significant differences between randomization groups at baseline. Global cognitive scores improved significantly within all of the groups (mean change: 0.16 standard deviations [SD]; all $p<0.05$) but did not differ between the

mental activity groups (p=0.19) or exercise groups (p=.65). There was a significant interaction (p=0.02) with baseline memory in which the mental activity training groups did not differ for subjects with normal memory scores at baseline (p=.82) while subjects with low memory scores at baseline benefited significantly more from the Posit Science than the educational DVD training (p=0.02).

Conclusions: Different physical and mental activity interventions are associated with similar improvements in global cognitive function in older adults with cognitive complaints. Individuals with poor memory may especially benefit from more intensive mental activity training.

#25

Tonic and Phasic Attention Training Improves Working Memory and Executive Function in Normally Aging Participants. Ativ Zomet[1], Christina Marini[1], Thomas Van Vleet[1]; [1]Brain Plasticity Institute, San Francisco - A number of recent studies indicate that attention training focused on the promotion of a more optimal attentional state (i.e., by exercising vigilance and sustained-attention) can improve deficits in higher-order functions such as working memory and executive control. These higher-order deficits are a primary concern for the many millions of individuals experiencing age-related cognitive decline. Our own studies in acquired brain injury patients suffering from poor attention regulation were among the first to demonstrate that relatively brief daily epochs of Tonic and Phasic Alertness Training (TAPAT) produces lasting benefits that endure for weeks in the absence of additional training (see DeGutis & VanVleet, 2010; VanVleet et al., 2010; Van Vleet & DeGutis, in review). In the current study, we examined the effects of TAPAT training in participants from a normally-aging population. Pre and post nine, 24-minute sessions of TAPAT training, participants were assessed on neuropsychological and psychophysical measures of cognition and mood regulation (i.e., attention, working memory, executive function). The training intervention required participants to detect a randomly occurring target object (10% of trials) in a continuous stream of distracter objects presented at fixation. Patients were required to continually make responses to all but the target object during two back-to-back 12-minute blocks. Pre vs. post-training assessment performance revealed significant improvement in attention & working memory (e.g., sustained and selective attention), executive function (e.g., span, divided processing, generative fluency). The results suggest that training the attentional state may provide beneficial improvement across a number of attentional and cognitive processing domains.

#26

Training age-related multitasking deficits in older adults through an action driving video game. Joaquin A. Anguera[1], Jacqueline Boccanfuso[1], Jean L. Rintoul[1], Omar Al-Hashimi[1], Erwin Kong[1], Yudy Cristo[1], Farshid Faraji[1], Radwa Moustafa[1], Eric Johnston[1], Adam Gazzaley[1]; [1]University of California, San Francisco - Older adults exhibit working memory deficits beyond that of younger adults in the setting of distractions (irrelevant stimuli) and interruptions (attended stimuli as an aspect of a secondary task - multitasking). Here, we designed a novel car driving video game that challenged distraction and multitasking abilities by integrating a target discrimination task and visuospatial tracking task. This game served as a training intervention to mitigate age-related deficits in interference processing. 24 older adults (61-80) were equally divided into a multitasking training, single task training, and a no contact control group. Training took place at home in twelve 1-hour sessions over the course of a month. Both training groups showed comparable training-related effects in their visuomotor tracking and target discrimination abilities. However, multitasking training resulted in a significant reduction in multitasking cost compared to single task training ($p < .02$) and the no contact control ($p < .01$) as evaluated with an experimental version of the game pre- and post-training. This improvement was not the result of better single task performance, as this changed equivalently in each group ($p > .25$). Thus, preliminary findings suggest that the use of this novel, cognitive platform was effective as a intervention to mitigate age-related interference effects in older adults. In addition to doubling the total number of participants, subsequent analyses involve electroencephalography (EEG) recordings obtained during the experimental version of the game and an extensive battery of cognitive assessments to quantify the neural mechanisms underlying these age-related interference effects as well as transfer to other cognitive abilities.

#27

Evaluation of a novel neuro-plasticity based auditory training program to remediate top-down cognitive control deficits in healthy aging. Jyoti Mishra[1,2], Aneesha Nilakantan[3], Michael Merzenich[2], Adam Gazzaley[1]; [1]UC San Francisco, [2]Brain Plasticity Institute, [3]UC Berkeley - Older adults demonstrate significant deficits in the resolution of goal-relevant information from irrelevant information across the cognitive faculties of perception, attention and working memory. We developed a novel training strategy to specifically address these deficits, and tested its first implementation in the auditory domain. The training required individuals to seek out and retain identity of a low probability tone-frequency target amidst many distracting tones of variable frequencies (0.2-4kHz), over a timespan of multiple minutes. The training was generalized to multiple target tones across the audible spectrum & incorporated trial-by-trial performance feedback. It was also continuously adaptive in that the distracting tone frequencies approached the target frequency as the trainee progressively performed more accurate target-distractor discriminations. Healthy older adults (n=9, age 60-90 yrs.) trained at-home on a computerized web-based platform for 1 month (12 0.5-hour sessions), immediately preceded and followed by in-lab neuropsychological and neural (EEG-based) assessments. An age-matched no-contact control group (n=10) was included. Learning associated changes included improvement in auditory discrimination thresholds and significant improvement in working memory letter-number span measures. Although tests of sustained attention and working memory with interference did not show significant changes, improvements on the training task were directly correlated with incremental improvements on these assessments. Neural data showed significant reduction of distractor-evoked auditory potentials, as well as enhancement of midline frontal theta oscillations for relevant targets. Overall, our results showcase a promising new training strategy that induces significant neuroplasticity in the aging brain, and has the potential to address age-related cognitive control deficits.

#28

Aging, perceptual learning, and changes in efficiency of motion processing. Jeffrey D. Bower[1], George J. Andersen[1]; [1]University of California, Riverside - In the present study we examined the use of perceptual learning to improve motion processing in older and younger individuals. Using the Perceptual Template Model (Lu & Dosher, 1998; 1999), age-related differences in baseline perceptual inefficiencies and changes due to training were assessed for additive internal noise, tolerance to external noise, and internal multiplicative noise. In Experiments 1 and 2 we trained participants by manipulating contrast in noise embedded sine-wave gratings and Random Dot Cinematograms (RDCs). The results indicate that older observers have higher additive internal noise and lower tolerance to external noise

compared to younger observers. The rate of perceptual learning in older observers was found to be similar to that of younger observers suggesting that plasticity of motion processing mechanisms is well preserved in advancing age. Experiment 3 examined transfer of learning between sine-wave gratings and RDCs for both older and younger observers. The results indicate that transfer of learning occurred for both age groups. This suggests that older individuals maintain a sufficient degree of plasticity to allow generalization between sine-wave gratings and RDCs. In addition, training with RDCs was found to produce greater perceptual learning than training with sine-wave gratings. The present studies provided important findings regarding changes in perceptual efficiency for motion perception in older adults and suggest that perceptual learning is an effective approach for recovering from age-related declines in visual processing.

#29

Comparing the Effectiveness of Cognitive Stimulation and Adaptive Training Techniques Among Older Adults.. Elise G. Valdes[1], Carol L. Peronto[1], Jennifer L. O'Brien[1], Jessie Alwerdt[1], Jerri D. Edwards[1]; [1]University of South Florida - Research has shown that although cognitive performance tends to decline with age, cognitive stimulation may protect against decline (e.g. Hertzog, Kramer, Wilson, & Lindenberger, 2009). Other researchers have suggested that specific, adaptive cognitive training may be necessary to obtain cognitive improvements (e.g., Valenzula & Sachdev, 2009). We compared an adaptive cognitive training program, standardized cognitive training program, internet training, and a no contact control condition in order to examine whether cognitive stimulation is a mechanism for cognitive training gains as measured by the Useful Field of View Test (UFOV), a measure of processing speed and attention. A total of 278 adults between the ages of 62 and 95 participated in two studies of cognitive training (Edwards et al., 2002; Edwards, et al., 2005). A 4x2 mixed-model Analysis of Variance was conducted to determine the effect of different cognitive training conditions (adaptive vs. standard vs. internet training vs. no contact control) and time (pre- vs. post-training) on UFOV performance. Results indicated significant main effects of time, $F(1,252)=276.80$, $p < .001$, training group, $F(3,252)= 13.59$, $p < .001$ and a group x time interaction, $F(3,252)= 32.32$, $p < .001$. Only the adaptive training group performed significantly better than either the internet training group or no contact control group, who performed similarly. No other significant differences were found. These results suggest that adaptive training may be most beneficial for improving older adults'speed of processing, and that cognitive stimulation, such as internet training, does not immediately improve UFOV performance.

#30

Improving Speed of Processing and Attentional Allocation in Older Adults via Cognitive Training. Jennifer L. O'Brien[1,2], Jennifer L. Lister[1], Jerri D. Edwards[2], Nathan D. Maxfield[1], Victoria A. Williams[1], Carol L. Peronto[2], Elizabeth M. Gagnon[2], Elise G. Valdes[2], Chelsea McNee[1]; [1]Department of Communication Sciences and Disorders, University of South Florida, [2]School of Aging Studies, University of South Florida - It is well established that older adults experience decline in cognition, including slowed speed of cognitive processing and attention switching (Madden et al., 2005; Salthouse, 1996). InSight training is a behavioral cognitive intervention involving computerized attention and memory tasks designed to enhance the speed and efficiency of visual processing. Here, we investigate the effectiveness of InSight training to improve older adults' neural system functioning. Before and after 20 hours of training using the InSight program, event related potentials (ERP) were recorded while older adults completed a visual search task. Amplitude and latency of the P3 and N2pc components were examined from the trained group and compared with a control (untrained) group to determine whether InSight training increased processing speed and/or enhanced attentional resource allocation. Both P3 and N2pc components are useful in understanding the relationship between cognitive decline and aging, as both are known to decrease in amplitude and increase in latency with age, reflecting age-related slowing of stimulus evaluation processes and a reduction of attentional resource allocation. Preliminary results ($n = 19$) indicate that InSight training increases the amplitudes of both the P3 ($p < .01$) and N2pc ($p = .11$). Results suggest that InSight training enhances both visual processing speed and the allocation of attention to relevant stimuli in older adults.

#31

Divided Attention Gains Mediate Transfer of Speed of Processing Training to Everyday Functioning. Jerri Edwards[1], Christina Ruva[2], Christine Haley[1], Elizabeth Hudak[1]; [1]University of South Florida, [2]University of South Florida Sarasota-Manatee - Although several interventions improve older adults'cognition, few have transferred beyond the skills practiced in training. Speed of processing training (SOPT) is one intervention that has transferred to improved functional abilities (e.g., Ball, Edwards, & McGwin, 2010). However, the underlying mechanisms of training transfer are not known. Mediation analyses are one way to examine potential mechanisms of cognitive training. SOPT is a computerized, cognitive intervention aimed at enhancing Useful Field of View (UFOV) performance, which assesses speed for visual attention tasks (Edwards, et al., 2005). In a prior study, older adults (N=126) between the ages of 62-95 years were randomized to SOPT or an active control condition. SOPT transferred to improved performance on the Timed Instrumental Activities of Daily Living Test (TIADL), a measure of everyday functional performance (Edwards et al., 2005). We use mediation analyses to examine whether these TIADL performance improvements can be directly attributed to cognitive improvements in UFOV due to training. Bootstrap analysis was used to test our meditational model of X->M->Y (where X is SOPT, Y is TIADL, and M is UFOV). The indirect effect of UFOV performance significantly mediated the training effect on TIADL performance, with point estimates (ab) of .20 and CIs 95% of 0.02 to 0.41. Results indicate that cognitive training gains in the divided attention subtest of UFOV completely mediated the transfer of SOPT to everyday functional performance. Improving divided attention may be particularly important to positively affect everyday functioning.

#32

Creative Designs for Healthy Minds. Michael Zelin[1], Stephen Gemmell[2], Suzanne Fitzsimmons[3]; [1]Adan, Inc., Fayetteville, AR, [2]Memory Clinic, Washington Regional, Fayetteville, AR, [3]Sunset Hills Aging & Wellness, Inc., Greensboro, NC - Computer based recreational therapy (RT) systems have been shown to be effective for cognitive exercises. The goal of our Creative Designs for Healthy Minds (CDHM http://www.SeniorCreativity.com) project was to develop a new online RT system providing cognitive activities for senior users (65+) through creating online multimedia compositions. We used a new approach to leverage benefits of arts-, creativity-, and digital storytelling- based therapies and the World Health Organization Quality of Life Assessment Instrument (WHOQOL-100) to asses CDHM. The system provides new incentives for engaging seniors in cognitive activities: i. meaningful enjoyment from creative activities yielding socially valuable results as compared with repetitious actions in existing RT games; ii. serious game format including puzzling together existing pieces of text, music, sound, and video-files, incorporating authors' original

pieces, and reality game utilizing format of a Role Playing Game (RPG) Forum; iii. online competitions with a complete Content Management System (CMS) including simple tools for user management, customizing competition web pages, adding resources, sponsors, partners, and judging online; iv. novel mechanisms rewarding creativity, collegeal behavior, and community service, such as support of non-profit organizations, including those using arts for RT. Assessment of the system indicates that it could be a new effective tool for cognitive exercises leveraging existing online arts and RT resources.

#33

Self-efficacy for Computer-Based Cognitive Remediation in Alzheimer's disease. Jacqueline Helcer[1], Gennarina Santorelli[1], Jimmy Choi[1]; [1]Columbia University Medical Center - Introduction: Cognitive remediation (CR) for Alzheimer's disease (AD) is becoming more readily available to the geriatric population in an attempt to curb the insidious decline in cognitive and functional performance. Patients with dementing pathology, however, may have difficulty adhering to these cognitive treatments due to denial of memory deficits, lack of motivation and apathy, or a sense of hopelessness which may be primarily due to illness or secondary to geriatric depression. For this reason, remediation techniques which incorporate motivational strategies to enhance treatment engagement and self efficacy may provide greater benefits than standard remediation training. Methods: Sixty-nine outpatients diagnosed with mild to moderate Alzheimerâ's disease were randomly assigned to 3 months of (1) memory training (MT), or (2) Cognitive Vitality Training (CVT), the same memory training but contextualized in a milieu specifically designed to increase adherence to treatment by enhancing motivation and self efficacy and empowering patients to be actively involved in treatment. Assessments of cognitive function, quality of life, neuropsychiatric symptoms, activities of daily living, treatment adherence, motivation, and perceptions of self efficacy were conducted at intake, 2, 4, and 6 months. Results: Patients in CVT showed greater resistance to memory decline compared to MT at 6 months. Patients and caregivers in CVT both reported better quality of life and less overall depressive symptoms throughout the intervention. Interestingly, perceptions of self efficacy predicted cognitive outcome, even after variance attributable to group assignment, baseline memory ability, overall dementia symptoms, and depressive symptoms were accounted for. Conclusion: This suggest that while patients recently diagnosed with AD (and their caregivers) experience a tremendous loss of control in their lives, therapies which strive to re-introduce elements of control and self-efficacy through intrinsic motivation may offer psychological as well as neuropsychological benefits. Applying these findings to a more preventive approach in the prodromal stages of dementia (mild cognitive impairment) will also be discussed.

#34

Keep me independent and driving: The transfer of using a computerized cognitive training program to maintain driving mobility across five years in older adults. Lesley A. Ross[1], Jerri D. Edwards[2], Karlene K. Ball[1], David L. Roth[1]; [1]University of Alabama at Birmingham, [2]University of South Florida - Many cognitive abilities are modifiable throughout the lifespan; however, the transfer of cognitive training to everyday activities has yielded mixed results. Driving is one everyday activity that is strongly related to cognitive capacity and is of great importance to older adults. Processing speed (via the Useful Field of View, UFOV) is a modifiable cognitive ability that is associated with driving competence and mobility. Longitudinal mixed models investigated the impact of a computerized processing speed training program through Intention-To-Treat (ITT) and exposure (treatment-received) analyses on three self-reported driving behaviors of older adults over a five-year period from the ACTIVE randomized clinical trial (N=1806). Processing speed participants were compared to those in the no-contact control group. No significant effects were found within the ITT analyses or the treatment-received analyses within the total sample. However, transfer occurred in a subsample of persons at-risk for mobility decline (e.g., poor initial processing speed via UFOV; n=239). Among this subsample, participants who received more training sessions maintained their driving frequency and those who received additional booster sessions reported greater maintenance of both driving frequency and exposure over time, Ps<.05. Additional analyses investigated the potential impact of socialization/social-contact on subsequent driving through a similar comparison of at-risk participants who had been randomized to another non-computerized cognitive training group to the no-contact control group(n=234). There was no impact of this non-computerized training on driving via ITT or treatment-received analyses. Results of this study indicate a real-world impact as a result of 8-18 hours of a computerized training program.

#35

Perceptual Training Overcomes the Optical Deterioration of the Aging Eye. Maria Lev[1], Uri Polat[0], Anna Sterkin[0], Oren Yehezkel[1], Ativ Zomet[1], Jian-Liang Tong[3], Clifton Schor[3], Dennis Levi[3]; [1]Tel-Aviv University, Tel-Aviv, Israel, [2]Ucansi Inc. NY, USA, [3]UC Berkeley – Purpose : In presbyopia (aging eye), the visual input to the brain is blurred due to the deteriorated optics of the eye. Thus, near vision is affected starting at age of 40 years. We investigated whether improvement in the brain functions found after perceptual learning changes the optical functions as well.

Methods: We used a personalized training method (Ucansi Inc.), posing spatial and temporal constraints on the visual processing. Visual acuity, spatial and temporal contrast sensitivity, contrast discrimination and reading speed were tested before and after the treatment. Accommodation, depth of focus and pupil size were also measured before and after training. Subjects practiced at least twice per week, from a distance of 40 cm. The study was performed at the University of California, Berkeley, and included 30 presbyopic and 7 control young subjects.

Results: After training, significant improvement in spatial and temporal contrast sensitivity, contrast discrimination and reading speed was found, reaching the level of the young group. Visual acuity improved by â‰ˆ 81%, equivalent to a decrease in effective age of about 8 years. Reading speed of the small letter size improved by â‰ˆ 4 seconds per sentence, gaining 3-5 minutes per page. Subjects were able to read and perform near activities without reading glasses. No changes in accommodation, pupil size or depth of focus were found.

Conclusions: Training produced substantial perceptual improvements (detection, discrimination) that generalized to cognitive functions, such as reading speed and decision reaction time, with no changes in eye optics.

#36

The influence of age and education on cognitive plasticity in a worldwide sample of 88,000 individuals. Benjamin Katz[1], Tieming Ji[0], Joseph L Hardy[1], Michael Scanlon[1]; [1]Lumos Labs, [2]Iowa State University - Recent findings (e.g., Jaeggi, et al. 2011) suggest a positive relationship between transfer effects following cognitive training and improvements on the training task itself. Uncertainty remains regarding the drivers of individual differences in response to cognitive training. An improved understanding of these factors would have important implications for future experimental design as well as practical implementation of cognitive training programs. We

hypothesize that a significant proportion of the variance across individuals in training improvement can be explained by age and education. We constructed a speeded verbal fluency training task where participants are required to type as many words as possible using a three letter stem. Data were drawn from a geographically and demographically diverse sample of over 88,000 individuals aged 15 - 75 who completed at least 25 training sessions with the task, which is freely available on the website lumosity.com. An analysis of performance revealed that while individuals across the entire age and education spectrum showed improvements with training, users younger than 35 years of age or with a Ph.D. education improved at a faster rate, while users older than 65 years of age or with only a high school education improved more gradually. These results are consistent with the hypothesis that neuroplasticity is mediated by lifespan development and experience, and suggest that more intensive cognitive training may be required for older and less educated individuals in order to see equivalent benefits to those experienced by younger and more educated individuals.

Traumatic Brain Injury/Neurological Impairment

#37

Training Executive Functions with Verbal Fluency in Traumatic Brain Injury: Preliminary Results. **Son Preminger[1,2], Maayan Wertman[0], Yael Bogen[0], Eyal Heled[0], Elena Itskovich[2], Hila Zigdon[2], Assaf Loya[2], Rafi Malach[2], Eugenia Agranov[3,5]; [1]School of Psychology, Interdisciplinary Center Herzliya, Israel., [2]Neurobiology Department, Weizmann Institute of Science, Rehovot, Israel., [3]The day treatment rehabilitation unit - Sheba medical center, Tel ha Shomer, Israel., [4]Psychology Department, Hebrew University, Jerusalem, Israel, [5]Faculty of Medicine, Tel Aviv University, Israel** - Disorders of executive functions are common after traumatic brain injury (TBI) involving the frontal lobes, in particular disorders of self-generation and self-initiation. Cognitive rehabilitation methods for these dysfunctions are scarce. Here we present a novel training procedure which is based on the Verbal Fluency task, a task extensively used for assessment of prefrontal function and self-generation of response. Our training aims at repeatedly providing a constrained setting that encourages self-initiation of novel purposeful thought processes. Preliminary results of our study of this method are presented.

Five participants with apathy subsequent to moderate-to-severe TBI were recruited based on clinical evaluation and apathy questionnaires. Training constituted 10 daily sessions of 20-45 minutes, performing a trial-based version of the Verbal Fluency task. A battery of behavioral tests and neuropsychological assessments was performed before and after the training to evaluate the effect of training and its transfer to other tasks. Our preliminary results show that overall there was a gradual decrease in average time per word generation along training sessions, with results possibly depending on type of brain injury. Preliminary analysis of pre/post tests suggests that improvement in assessment battery tasks was consistent with improvement during training. Further analysis and experiments are required to evaluate the full potential of this method.

#38

VESTPA: Visually Enhanced Speech Treatment for Persons with Aphasia. **Paul Fillmore[1], Jessica Richardson[1], Johann Fridriksson[1], Julius Fridriksson[1]; [1]University of South Carolina** - Stroke is the leading cause of adult disability in the United States, and it is estimated that approximately one million Americans suffer from chronic aphasia due to stroke. Furthermore, most gains in function are made within the first few months post-stroke. As a result, availability of treatment for aphasic patients rapidly decreases after this period. However, recent work from our laboratory (Fridriksson 2010) demonstrated that significant gains can be made, even as many as twenty years post-stroke. In this study, as in most aphasia treatment, we used intensive production-based anomia treatment. However, we have also recently demonstrated (Fridriksson et al., 2009) that treating speech perception (using a word-picture matching paradigm) can have a significant effect on improving speech production, as measured by correct picture naming. Furthermore, the addition of visual speech cues to auditory-only treatment significantly improved treatment outcome. The current work presents an ongoing project in which we have implemented visual speech treatments and incorporated several new modules (phonemic, phonological, lexical, semantic, graphemic and syntactic) that will treat various aspects of speech and language, which we hope will generalize to improve function in both speech perception and production. Most importantly, this work will be implemented as a freely available web-based program, extending treatment to chronic aphasics for whom it had been previously unavailable.

#39

Speed of information processing neurorehabilitation program: A pilot study of adults with traumatic brain injury. **Gerald T. Voelbel[1], Joseph Rath[2], Teresa Ashman[2], Tamara Bushnik[2], Stan Fort[1], Laura Miles[2], Coralynn Long[2], Kristin Szostek[1]; [1]New York University, Steinhardt School, Department of Occupational Therapy, [2]New York University, Rusk Institute for Rehabilitation** - One of the most frequent cognitive deficits associated with traumatic brain injury is speed of information processing (SIP) deficits. This pilot study exams the utility of a computerized program, Brain Fitness Program (BFP) as a method of cognitive rehabilitation for SIP deficits in adults with severe TBI. In addition, this study investigates if increases of cognitive abilities can be detected in domains such as executive function, verbal memory, visual memory, working memory, and concentration. Adults between the ages of 18 and 65 years old who acquired a TBI were included in the study. After entering the study, participants underwent a neuropsychological battery that included the CNS-Vital Signs neuropsychological battery, Paced Auditory Serial Addition Test, Trail Making Test- A & B, Wisconsin Card Sort Test-CV, Beck's Depression Inventory-II, and Beck's Anxiety Inventory. Following the neuropsychological battery, the participants underwent 40 hours of training on the BFP software over a 12 week period. After completing the BFP the participants underwent the neuropsychological battery again to detect changes in performance. The results demonstrated the TBI group that underwent the BFP intervention improved up to 27% on SIP above baseline. A 16% and 18% improvement over baseline was also revealed in verbal and visual memory, respectively. Working memory and executive functioning demonstrated a 20% and 22% improvement, respectively. This study demonstrates improvements in SIP deficits can be remediated in adults with TBI. In addition, these results suggest cognitive improvements are not restricted to SIP, but can be detected in other cognitive domains, as well.

Schizophrenia

#40

Restoring Reality Monitoring in Schizophrenia: Behavioral and fMRI Assessments. **Karuna Subramaniam[1], Tracy Luks[2], Melissa Fisher[1], Gregory Simpson[2], Srikantan Nagarajan[2], Sophia Vinogradov[1]; [1]San Francisco Department of Veterans Affairs Medical Center and Department of Psychiatry, University of California, San Francisco, CA, [2]Department of Radiology and Biomedical Imaging, University of California, San Francisco** - Schizophrenia

patients suffer from severe cognitive deficits, such as impaired reality monitoring. Reality monitoring is defined as the ability to distinguish the source of internal experiences from outside reality. During reality monitoring tasks, schizophrenia patients make errors identifying "made it up" items, and even during accurate performance, they show abnormally low activation of medial prefrontal cortex (mPFC), a region that supports self-referential processes. In the present study, we investigated whether this deficit is amenable to a behavioral intervention.

Thirty one schizophrenia patients and 15 healthy control subjects underwent an fMRI reality monitoring task at baseline in which subjects had to decide whether target words were previously self-generated or experimenter-presented. Patients were then randomly assigned to either 80 hours (i.e.,16 weeks) of neuroscience-informed computerized cognitive-training that focused on training auditory, visual and social cognitive processes, or to a control condition of 80 hours of computer-games. All subjects repeated the task after the 16 week intervention period.

After 16 weeks of active training, schizophrenia patients showed significant improvement in reality monitoring that correlated with increased mPFC activity. In contrast, patients in the computer games control condition did not show any neural or behavioral improvements. Remarkably, recovery in mPFC activity after training was associated with improved verbal memory recall, and with better social functioning six months later.

These findings demonstrate that a serious behavioral deficit in schizophrenia, and its underlying neural dysfunction, can be improved by well-designed cognitive training, resulting in improved quality of life.

#41

Predictors of Response to Computerized Neuroplasticity-Based Cognitive Training in Schizophrenia. **Melissa Fisher[1,2], Karuna Subramaniam[0], Phillip Alexander[0], Coleman Garrett[0], Sophia Vinogradov[0]; [1]Department of Psychiatry, University of California, San Francisco, [2]San Francisco Department of Veterans Affairs Medical Center** - We have previously reported interim findings from our RCT of computerized, neuroplasticity-based cognitive training in schizophrenia. Here, we report the final behavioral results and explore predictors of response to treatment. Forty subjects completed 50 hours of neuroplasticity-based auditory training and were compared to 34 subjects who completed an equal number of hours of computer games. A subset of subjects also completed fMRI, measures of insight into cognition (MIC-SR) and theories of intelligence (TOI). Pearson-correlations were conducted to: 1) Assess whether better cognitive performance was associated with change in fMRI signal within the right dorsolateral prefrontal cortex (R.DLPFC) during a 2-back working-memory task; 2) Determine the relationship between baseline self-report measures with gains in MATRICS-recommended cognitive domains. Cognitive training subjects showed significant gains in Global Cognition, Speed of Processing and Verbal Learning and Memory, and a strong association between increased R.DLPFC signal and better Global Cognition and Verbal Learning and Memory after training, an association not seen in the computer games subjects. Participants with greater insight into their cognitive deficits and a stronger belief in the malleability of intelligence showed greater cognitive gains, even when controlling for baseline cognition and hours of training. These results show that: 1) Individuals with schizophrenia can make significant gains in cognition after intensive computerized training, even after an average of 20 years of illness; 2) Improved neuropsychological performance after training is correlated with training-induced increases in prefrontal cortical activity; 3) Psychological factors, such as insight and internalized beliefs about intelligence, affect the response to training.

#42

Normalization of high gamma band activity following cognitive training in patients with schizophrenia. **Ethan Brown[1], Alexander Herman[1], Corby Dale[0], Anne Findlay[1], Leighton Hinkley[1], Sophia Vinogradov[2,4], Srikantan Nagarajan[1]; [1]Dept. of Radiology and Biomedical Imaging Univ. of California, San Francisco, [2]Dept. of Psychiatry, Univ. of California, San Francisco, [3]NCIRE, [4]Dept. of Psychiatry, Veteran's Affairs Med. Ctr., San Francisco, CA** - Speech perception, memory and production are impaired in schizophrenia, and recent research shows that these deficits are amenable to intensive computerized cognitive training. We used 275-channel MEG to study cortical activity during both a syllable identification and a syllable reproduction task in 40 patients with schizophrenia. Subsequently, 22 patients underwent 50 hours of targeted cognitive training (TCT) that focused on auditory/verbal processes, while the remaining 18 spent an equal amount of time playing commercial computer games (CG), as a control. Time-frequency analysis and source localization using the NUTMEG spatially adaptive filter provided high spatial and temporal resolution of auditory and memory-encoding processing streams in multiple frequency bands (4-12Hz, 12-30Hz, 30-50Hz, and 63-117Hz). We compared changes in neural activity before and after TCT to changes before and after CG in patients with schizophrenia and to 14 matched healthy subjects. Controlling for performance, schizophrenia subjects at baseline showed lower power in the high gamma band in many areas, compared to healthy subjects. Cognitive training led to enhancement of high gamma activity in the TCT patient group, as compared to the CG group. This increase involved areas important for audiomotor processing, especially within the tempero-parietal junction and inferior frontal gyrus, and the resulting patterns of brain activity resembled what was seen in healthy subjects. In inferior parietal lobule, training-induced enhancement of high gamma correlated with task performance. These data suggest that intensive computerized training can normalize disrupted patterns of neural activity involved in auditory and verbal processing in schizophrenia.

#43

Changes in alpha band resting-state functional connectivity following computer-based training in patients with schizophrenia. **Leighton Hinkley[1], Sophia Vinogradov[0], Melissa Fisher[0], Ethan Brown[1], Corby Dale[1], Anne Findlay[1], Srikantan Nagarajan[1]; [1]Department of Radiology and Biomedical Imaging, University of California, San Francisco, [2]Department of Psychiatry, University of California, San Francisco, [3]Veterans Affairs Medical Center, San Francisco** - A growing number of neuroimaging studies have reported reduced functional brain connectivity in patients with schizophrenia both during behavior and at rest. Here, we use resting-state magnetoencephalography (MEG) to test the hypothesis that computer-based auditory training remediates functional connectivity in schizophrenia, and that these patterns of connections are directly related to recovery. Thirty clinically stable, chronically ill schizophrenia volunteers and fifteen healthy matched controls were enrolled and assessed with a standard neurocognitive battery of MATRICS-recommended measures. Fifteen participants from the schizophrenia group were enrolled in a computer-based auditory training program (Brain Fitness; Posit Science, San Francisco, CA) for a period of 40-50 hours over the course of 10-12 weeks Resting-state MEG data was collected using a 275-channel biomagnetometer (VSM MedTech). A single epoch of artifact-free data was selected and neural activity in the alpha range (8-12Hz) was estimated using an adaptive

spatial filtering technique. Resting-state functional connectivity was computed using imaginary coherence (IC). Within-group (pre-training vs. post-training) comparisons were evaluated using paired t-tests and functional connectivity maps were regressed against MATRICS measures. In the training group, increases in resting-state alpha IC were observed post-training over pre-frontal cortex and the left medial occipital gyrus. No significant differences in functional connectivity were observed in either healthy controls or the computer games control group. In an independent analysis, low functional connectivity of regions of left pre-frontal cortex predicted high change scores in measures of global cognition. These neuroimaging-based markers have the potential to track recovery following cognitive-based rehabilitative paradigms.

#44

Latency of the acoustic startle response is slower in schizophrenia subjects than in healthy controls. Erica Duncan1,2, Wendy Hasenkamp0, Robin Gross0, Amanda Green0, Lisette Wilcox1, William Boshoven1, Barbara Lewison1,2; 1Atlanta VAMC, 2Emory University School of Medicine - Background: The acoustic startle response (ASR) is a reflex contraction of the skeletal muscles in response to a sudden acoustic stimulus. It is mediated by a simple 3-synapse subcortical circuit, and modulated by several cortical and subcortical areas. In humans the ASR is easily measured as the amplitude and time course of the eyeblink component of the startle response. Latency, the time from the startling acoustic stimulus to the onset of the ASR, is stable across time, highly heritable, and provides an index of the speed of neural processing. The purpose of the current study was to compare latency in schizophrenia (SCZ) vs. healthy control (CONT) subjects.

Methods: We tested 99 SCZ and 76 CONT subjects in a standard paradigm designed to evaluate the magnitude and latency of the ASR along with prepulse inhibition (the inhibition of the ASR by a preliminary nonstartling stimulus delivered just prior to the startling stimulus, used as an operational measure of sensorimotor gating in studies of SCZ). The eyeblink component of the ASR was measured via electromyography of the right orbicularis oculi muscle.

Results: Latency was significantly longer (i.e. slower) in SCZ than CONT subjects after controlling for age, race, and sex ($F(1,170)=5.39$, $p=0.02$). Antipsychotic medication treatment at time of testing did not significantly affect latency ($F(3,92)=0.71$, $p=0.6$).

Conclusions: SCZ subjects had prolonged latency, indicating a slowing of their neural processing through the 3-synapse startle circuit. Future studies will evaluate the ability of computerized cognitive training to normalize startle latency in SCZ.

#45

Feasibility and Pilot Efficacy Results from the Multi-site Cognitive Remediation in the Schizophrenia. Richard Keefe[1], Sophia Vinogradov[2], Alice Medalia[3], Peter Buckley[4], Stanley Caroff[5], Deepak D'Souza[6], Phillip Harvey[7], Karen Graham[8], Robert Hamer[8], Stephen Marder[9], Del Miller[10], Stephen Olson[11]; [1]Duke University Medical Center, [2]University of California San Francisco, [3]Columbia University College of Physicians and Surgeons, [4]Medical College of Georgia, [5]Veterans Affairs Medical Center, University of Pennsylvania School of Medicine, [6]Yale University School of Medicine, [7]University of Miami Miller School of Medicine Miami VA Medical Center, [8]University of North Carolina at Chapel Hill, [9]Semel Institute at UCLA & VA Desert Pacifc Mental Illness Research, Education, and Clinical Center, [10]University of Iowa, [11]University of Minnesota - Background: The true benefit of pharmacological intervention to improve cognition in schizophrenia may not be evident without regular cognitive enrichment. Clinical trials assessing the neurocognitive effects of new medications may require engagement in cognitive remediation exercises to stimulate the benefit potential. However, the feasibility of large-scale multi-site studies using cognitive remediation at clinical trials sites has not been established. Methods: Patients from nine sites were randomized to the PositScience auditory training program with weekly NEAR 'bridging groups,' or a control condition of computer games and weekly healthy lifestyles groups. Patients were expected to complete 3-5 one-hour sessions weekly for 40 sessions or 12 weeks, whichever came first. Results: The primary outcomes were feasibility results as measured by rate of enrollment, retention, and completion rate of primary outcome measures. Within the 3-month enrollment period, 53 of a projected 54 patients were enrolled and 47 completed the study. Thirty-one patients completed all 40 sessions and all patients completed all primary outcome measures. Preliminary efficacy results indicated that after 20 sessions, patients in the auditory training treatment condition demonstrated mean MCCB composite score improvements that were 3.7 (95% CI: 7.34, 0.05) T-score points greater than in patients in the computer games control group ($F=4.16$, $df=1,46$, $p=0.047$). At the end of treatment, a trend favoring auditory training was not statistically significant ($F=2.26$, $df=1,47$, $p=0.14$). Discussion: Multi-site clinical trials of cognitive remediation using the PositScience auditory training program with the NEAR method of weekly bridging groups in traditional clinical sites appear feasible.

#46

Cognitive Remediation Can Improve Social Functioning and Symptoms in Early Schizophrenia. Joseph Ventura[1], Keith Nuechterlein[1], Kenneth Subotnik[1], Denise Gretchen-Doorly[1], Laurie Casaus[1], John Luo[1], Morris Bell[2], Alice Medalia[3]; [1]UCLA, [2]Yale University, [3]Columbia University - **Background:** Meta-analyses report that cognitive remediation may include benefits for symptom reduction and improvements in functioning in chronic schizophrenia patients (McGurk et al., 2007; Wykes et al., 2011), but little is known about these potential benefits in the early course of schizophrenia. Methods: A randomized controlled trial compared cognitive remediation to another active intervention, healthy behavior training, in 60 patients with a first psychotic episode within the prior two years. Cognitive remediation combined approaches used in chronic schizophrenia by Morris Bell et al and Alice Medalia et al., drawn from neuropsychological rehabilitation and educational remediation fields, respectively. The BPRS, SAPS, SANS, and the UCLA Social Attainment Survey were used to assess changes in symptoms and social functioning.

Results: Cognitive remediation, as compared to healthy behavior training, resulted in a significant improvement from baseline to 6 months in global social functioning ($p=.023$). In particular there was a significant increase in Opposite Sex Peer relationships ($p=.002$) and in initiating social activities ($p=.037$). In addition, from baseline to 6 months, patients who participated in cognitive remediation as compared to healthy behaviors training showed a greater reduction in positive symptoms (reality distortion, $p=.01$) and tended to do so for negative symptoms such as anhedonia ($p=.056$).

Discussion: The beneficial effects of cognitive remediation might extend to improvements in social functioning and symptoms in recent-onset schizophrenia patients. These results suggest that cognitive remediation may have an impact in the early course of schizophrenia that reaches beyond cognition.

#47

Cognitive Training in the Early Course of Schizophrenia: Impact on Cognition and Work/School Functioning. Keith Nuechterlein[1], Joseph Ventura[1], Kenneth Subotnik[1], Gretchen-Doorly Denise[1], Laurie Casaus[1], John Luo[1], Morris Bell[2], Alice Medalia[3]; [1]UCLA, [2]Yale University, [3]Columbia University - **Background:** Cognitive remediation benefits cognition and sometimes also everyday functioning in chronic schizophrenia patients (McGurk et al., 2007; Wykes et al., 2011), but surprisingly little is known about the effect of cognitive training shortly after a first psychotic episode, when broad benefits might be expected to be even greater.

Methods: A randomized controlled trial compared cognitive remediation to another active intervention, healthy behavior training, in 61 patients with a first psychotic episode within the prior two years. Cognitive remediation combined approaches used in chronic schizophrenia by Bell et al and Medalia et al., drawn from neuropsychological rehabilitation and educational remediation fields. Twenty-two computer programs focused on attention, memory, and problem solving in 50 sessions. The MATRICS Consensus Cognitive Battery and the Global Functioning: Role Scale assessed change.

Results: Cognitive remediation, compared to healthy behavior training, resulted in a significant differential improvement from baseline to 12 months in the Overall Cognitive Composite Score for those who finished the 12-month protocol ($p < .05$) but not in an intent-to-treat analysis. Cognitive remediation led to significant differential gains in work/school functioning by 6 months ($p < .04$) that were sustained at 12 months ($p < .02$) in intent-to-treat analyses.

Discussion: Cognitive remediation improved cognition in recent-onset schizophrenia patients more than in a comparison group if they finished a 12-month protocol, but cognitive training approaches need to be optimized to yield stronger effects across all patients. Strong generalization to work/school functioning improvements is found, encouraging further focus on cognitive training for first-episode schizophrenia patients.

#48

Genetic biosignatures associated with response to computerized cognitive training in schizophrenia. Rogerio Panizzutti[1], Steve Hamilton[2], Sophia Vinogradov[0]; [1]Instituto de Ciâncias Biomedicas, Universidade Federal do Rio de Janeiro, Rio de Janeiro, RJ, Brazil., [2]Department of Psychiatry, School of Medicine, University of California, San Francisco, CA., [3]San Francisco Department of Veterans Affairs Medical Center - Intensive computerized auditory training results in improved cognition for schizophrenia patients, but participants show variation in their cognitive gains and the biological factors that affect the response to training are unknown. Given the association between the BDNF, DISC-1 and COMT genes and cognitive functioning, we asked if functional variation in these genes impacts the response of schizophrenia patients to cognitive training. We genotyped 48 patients who completed cognitive training and analyzed the association between DNA variants in these three genes and cognition assessed at baseline and after training. We studied four continuous phenotypes: Verbal learning/memory performance at baseline, global cognition at baseline, and changes in these two measures after 50 hours of training. All phenotypes showed significant association with SNPs in the candidate genes DISC1, COMT and BDNF. The DISC1 SNP rs16854957 was positively associated with both verbal learning/memory and global cognition at baseline. The DISC1 SNP rs4658971 and the COMT SNPs rs2239393 and rs4646316 were positively associated with Verbal learning/memory at baseline and negatively associated with the change after training. In contrast, COMT SNP rs4633 was negatively associated with Verbal learning/memory at baseline and positively associated with the change after training. These data suggest that genotype influences the response to intensive cognitive training in schizophrenia, and indicate that cognitive training regimens may need to be personalized to the underlying biosignatures of each individual patient.

#49

Perceptual learning strongly improves visual motion perception in schizophrenia. Yue Chen[1], Dan Norton[2], Ryan McBain[3], Dost Ongur[1]; [1]McLean Hospital/ Harvard Medical School, [2]Boston University, [3]Harvard School of Public Health - Schizophrenia patients exhibit perceptual and cognitive abnormalities. Given that cognitive systems depend upon perceptual inputs, improving patients' reduced perceptual abilities may be an effective means of cognitive intervention. Visual motion processing is deficient in schizophrenia. In healthy people, motion perception can be enhanced through perceptual learning, but it is unknown whether this perceptual plasticity is available in schizophrenia patients. The present study examined the degree to which patients' performance on visual motion discrimination can be improved, using a perceptual learning procedure. While both schizophrenia patients and healthy controls showed decreased direction discrimination thresholds (improved performance) with training, the magnitude of the improvement was greater in patients (47% improvement) than in controls (21% improvement). The training also transferred to performance improvement in an untrained task "speed discriminationâ" though to a lesser degree. These task-specific and transferable perceptual training effects suggest that perceptual plasticity is rigorously present in schizophrenia and can be applied to develop bottom-up cognitive interventions for this mental disorder.

Regulatory Issues

#50

Regulatory Considerations for Cognitive Neurotherapeutic Software. Stasio Catherine[1], Wade Travis[1], Chan Sam[1], Mahncke Henry[1]; [1]Brain Plasticity, Inc. - A quandary shared by many developers of cognitive neurotherapeutics software is how to both classify neurotherapeutic software, and market it to, the specific populations for which it is designed and intended. Developers must consider that neurotherapuetic software may soon require development, testing and clearance within a more regulated environment than previously applied. The first step in evaluating this potential approach is determining whether or not the software under development meets the formal definition of a medical device. The European Union (Directive 93/42/EEC), Health Canada, and the US Food and Drug Administration generally define a medical device, including stand-alone software, as a product intended for use in the cure, mitigation, treatment or prevention of disease in man. Medical devices, including standalone software by this definition, would therefore be subject to the Federal Food, Drug and Cosmetic Act, which prohibit manufacturers, under penalty, from marketing or commercially distributing devices without specific marketing clearance or approval. As a result, manufacturers and developers of cognitive neurotherapeutic software may be well served to develop therapeutic software programs within an FDA-defined Quality Management System; and engage federal regulatory agencies in discussions regarding the construction, clinical testing, and regulatory submission and clearance procedure early on in the development cycle. We detail the specific steps involved in quality development processes, and the timing requirements of each, for use by developers or manufacturers who intend to commercialize neurotherapeutic software and market it to clinicians and/or patients with specific disease states or conditions.

GENERAL INFORMATION

Internet Access - Free Public Wireless Internet Access is available in the Robertson Auditorium for all attendees.

Grupio App - ESCoNs has set up a smartphone application that makes attending ESCoNs 2011 a lot more convenient and fun! It provides easy access to event information, schedules, maps, speaker information and a whole lot more to all Attendees.

For: **iPhone**, download "Grupio" from the app store.

Android, download "Grupio" from Android Market, ESCoNs event is listed in 3rd position.

Blackberry (Storm and Torch) but only if you have a touch screen device with OS 5.0 and above.

No SmartPhone, you can use the mobile application website at www.grupio.com/escons2011

Lost & Found - The meeting Lost and Found is located at the ESCoNS Registration Desk in the foyer of the Robertson Auditorium; any items left after Tuesday, September 20, will be left with the Mission Bay Conference Center lost & found.

Name Badges - For security purposes, attendees, speakers and exhibitors are asked to wear their name badges to all sessions and social functions; entrance into sessions is restricted to registered attendees only. If you misplace your name badge, please go to the Registration desk for a replacement.

Smoking – Mission Bay Conference Center is a non-smoking facility. Smoking is not permitted in or outside any of the meeting rooms.

Speakers - All speakers must register and wear name badge to present. Please ensure that you are available at least thirty minutes before the start of the session. Expense reports are available at the registration desk. Please submit any travel receipts no later than October 21 to be reimbursed for your expenses.

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TRANSPORTATION

ESCoNS Shuttle - We offer free shuttle service to/from the Hotel Palomar and Mission Bay Conference Center for all attendees. Shuttle will board in front of the Hotel Palomar at 12 Fourth Street, and in front of the Mission Bay Conference Center at 1675 Owens Street.

SHUTTLE TIMES

The shuttle can accommodate 30 people per trip.

Each of the times listed below are ESTIMATED departure times. Advance reservations for Monday are encouraged. Visit the registration desk for more information.

Hotel Palomar Departure Times

Shuttle will depart from the front of the hotel at 12 Fourth Street

7:00 am	8:30 am
7:30 am	9:00 am
8:00 am	9:30 am* last shuttle

MBCC Departure Times

Shuttle will depart from the front of the Convention Center at 1675 Owens Street

5:00 pm	7:10 pm
5:30 pm	7:30 pm
6:00 pm	7:50 pm * last shuttle
6:50 pm	

Muni - One block from the hotel located at the 4th and King Street Caltrain Station you can take the "T-Third Metro Line;" be sure to get off at the appropriate stop which is the "USCF Mission Bay Station" located on 3rd Street opposite the campus. You can also go to the Embarcadero BART station to catch the "T-Third Metro Line."

Taxi - Taxi ride from Hotel Palomar to MBCC is approximately 6-7 minutes at $8-10 per trip.

Walking - Mission Bay Conference is approximately 2 miles from the Hotel Palomar, directly south of Hotel Palomar on Fourth Street.

(A) Hotel Palomar San Francisco
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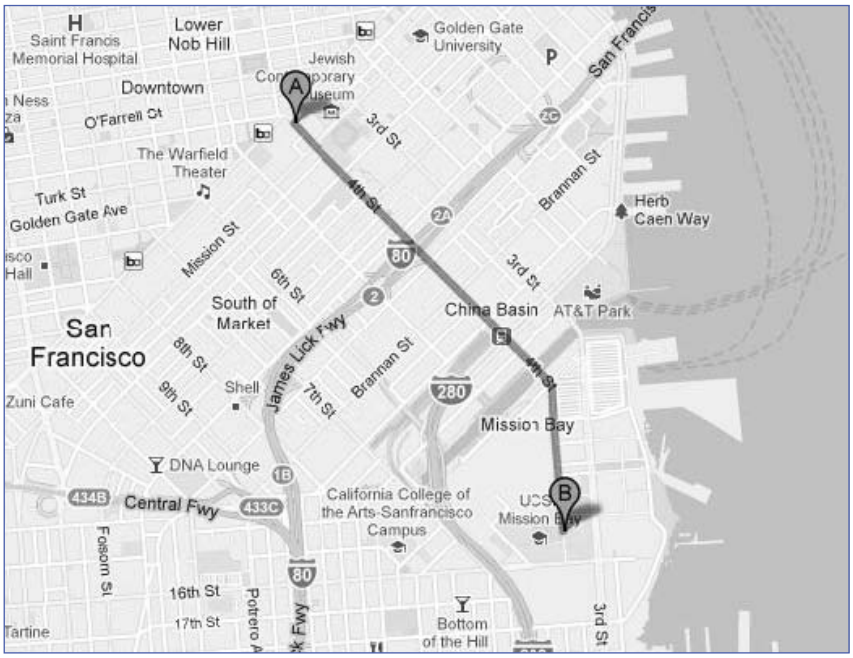

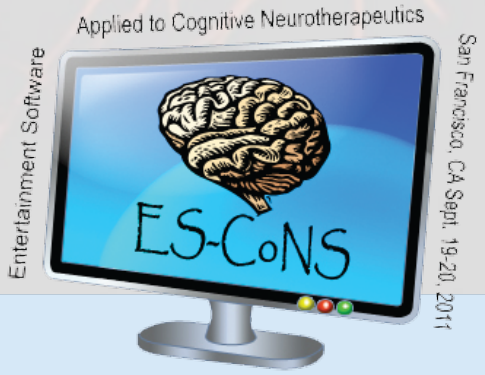

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