# The NKInformer



#### A newsletter of the Nathan S. Kline Institute for Psychiatric Research

Donald C. Goff, MD, Director Antonio Convit, MD, Deputy Director Thomas O'Hara, MBA, Deputy Director, Institute Administration

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Stuart Moss, MLS, Editor

### CENTER FOR DEMENTIA RESEARCH'S NEW ELECTRON MICROSCOPY LABORATORY IS NOW OPEN



Chris Goulbourne, PhD, joined the Center for Dementia Research as Electron Microscopy Director last November. Dr. Goulbourne obtained his B.Sc. from Durham University and his Ph.D. from Oxford University in molecular cell biology. He then went on to do an American Heart Association postdoctoral fellowship at UCLA where he specialized in electron microscopy techniques such as ultrastructural analysis, electron tomography, immunogold electron correlative light and microscopy, electron microscopy, and Nano Secondary Ion Mass Spectrometry (NanoSIMS). Before coming to NKI, he managed electron microscopy laboratories at GlaxoSmithKline and Columbia University.

Dr. Goulbourne has some new equipment at his disposal – a new electron microscope, microtome, and Vitrobot. Here are the details:

The FEI Talos L120C transmission electron microscope has the capability to do 2D imaging, dual axis electron tomography for 3D ultrastructural evaluation and cryogenic techniques. Services offered include ultrastructural evaluation in 2D and 3D based on a Bioquant VI system format, protein localization using immunogold techniques and cryogenic evaluation of proteins, viruses, and cellular architecture. Additionally, the facility offers advice and sample preparation for employing correlative light and electron microscopy (CLEM) and Nano Secondary Ion Mass (NanoSIMS) spectroscopy for tracking stable isotope tagged molecules.



**Talos Electron Microscope** 

Sample preparation instrumentation includes a Leica UCT ultramicrotome for sectioning samples and an FEI Vitrobot for cryo sample preparation of cells, viruses, proteins, and exosomes.



Microtome



Vitrobot

Installation of the new instruments was no small feat. Three tons of equipment were delivered in nine very large crates, and took three weeks to install.







#### **GRANTS RECEIVED**



National Institute of Mental Health

Christopher Cain, PhD (Emotional Brain Institute) received an R01 grant from NIMH entitled "<u>Brain</u> <u>Circuits of Outcome-dependent vs. Habitual</u> <u>Avoidance</u>". The award is through the NYU School of Medicine and is subcontracted to NKI, where work will also be carried out by **Robert Sears, PhD**.



Efrat Levy, PhD, Paul Mathews, PhD (Dementia Research), and Donald Wilson, PhD (Emotional Brain Institute) are Co-Principal Investigators on an RF1 NIA grant titled "Neuronal protective apolipoprotein E2-mediated endocytic and exocytic pathways". This application was in response to a request for applications from the NIA designed to fill in the significant gap in the field's understanding of why the apolipoprotein E2 allele is protective against Alzheimer's disease. The PI's wish to acknowledge that the application was greatly supported by preliminary findings by Kathy **Peng** during her graduate studies, by the efforts of Brett East and Gloria Fleming, and through NKI's mouse resources, supported in part by the efforts of Monika Pawlik and by Kathleen Shannon and the rest of the facility staff.



**Pamela Butler, PhD** (Clinical Research) is Co-Principal Investigator on an R61 award from NIMH entitled "<u>Visual Remediation in Schizophrenia</u>". The grant was awarded to Rutgers with a subaward to NKI. Public Health Relevance Statement: It has become increasingly clear that people with schizophrenia have visual impairments that affect

cognitive and social function in schizophrenia. The primary goal of the first phase of this project is to study the effects of two novel computer-based visual remediation interventions on visual perceptual deficits in schizophrenia. The primary goals of the second phase are to test the effectiveness of the optimal intervention on visual perception in a larger sample, and to test the link between improvements in visual perception and higher-level functions changes in specific (cognition, social function, and outcome) in preparation for a fully-powered clinical trial.

#### FROM AROUND THE INSTITUTE

### The New York Times

Helena Hansen, MD, PhD (Social Solutions and Services) was quoted in a <u>recent New York Times</u> <u>article</u> on racial disparities in opioid addiction treatment.



Joseph LeDoux, PhD (Emotional Brain Institute) was interviewed for the Dana Foundation's February <u>Cerebrum podcast</u>. Among other topics, Dr. LeDoux discusses "<u>Know Thyself: Well-Being</u> and <u>Subjective Experience</u>", the article he recently coauthored for Cerebrum.



**Charles Schroeder, PhD** (Biomedical Imaging and Neuromodulation) was quoted in <u>an article in *MIT*</u> *News*, about a recent paper published in *PNAS* by MIT researchers.

#### KUDOS



**Matthew Hoptman, PhD** (Clinical Research) has also joined the Editorial Board of *Schizophrenia Bulletin*. He now shares this role with Pamela Butler, PhD and Jean-Pierre Lindenmayer, MD.

#### **COMPLIANCE CORNER**



#### Single IRB Policy for Multi-Site Research

By Karya Ottey, PhD IRB Director

The National Institutes of Health (NIH) has instituted a policy on IRB review that effects all NIH-funded projects involving human subjects research conducted in the United States. This policy went into effect on January 25, 2018. The policy applies to multi-site studies in which each site will conduct the same protocol. *Researchers should be aware that the policy applies to all competing grant applications including new, renewal, revision, or resubmission.* 

An applicant that plans to submit for funding from NIH is expected to define a plan for the use of a Single IRB (sIRB) for Multi-Site Research. A sIRB is the primary IRB that will be responsible for the review and approval of all submissions from every site that will be an awardee of the grant. The use of a sIRB requires planning and collaboration between the investigators, institutions, and IRBs. Any researcher who plans to submit for NIH funding is required to submit a plan for sIRB. The plan should include:

- A detailed description of the plans to comply with using a sIRB.
- The name of the IRB that will serve as the sIRB.
- Confirmation statements from all identified participating sites to indicate agreement to rely on the proposed sIRB. This confirmation also needs to indicate that any sites added after award will rely on the sIRB.
- A brief description of the plans to facilitate communication between all sites and the sIRB.
- Confirmation from all participating sites that an authorization agreement will be finalized to clarify the roles and responsibilities of the sIRB and participating sites. The final authorization agreements do not need to be provided with the application.
- Clarification of which institution or entity will be required to maintain records of the authorization agreements and the communication plans.

Investigators that are using sIRB review are also required to consider the institutional fees associated with the reviews. Consultation will be required with each participating site to properly assign an IRB to serve as a sIRB and to account for any fees associated with the use of sIRB review. sIRB requires significant coordination between all the groups involved in the project. Investigators are urged to discuss any potential project with the IRB as soon as possible to better plan for which institution should serve as the sIRB and to facilitate the process with the local grant administrators at each institution.

For more information about the Single IRB Policy for Multi-Site Research, <u>see the NIH's FAQ's page</u>.

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#### **PUBLICATIONS OF NOTE**



Helen Scharfman (Dementia Research) published a paper on hilar mossy cells in *Cell & Tissue Research*.

Scharfman HE. Advances in understanding hilar mossy cells of the dentate gyrus. Cell Tissue Res. 2017 Dec 8. PMID: 29222692.



**Helena Hansen** (Social Solutions & Services) is a coauthor of this paper on racial, ethnic, and socioeconomic group differences in buprenorphine treatment.

Hatcher AE, Mendoza S, Hansen H. At the Expense of a Life: Race, Class, and the Meaning of Buprenorphine in Pharmaceuticalized "Care". Subst Use Misuse. 2018 Jan 28;53(2):301-310. PMID: 29161171.



**Crystal Lewis** (Social Solutions & Services) coauthored this paper on neighborhood context in drug injection behavior with colleagues at Columbia University.

DeCuir J, Lovasi GS, El-Sayed A, Lewis CF. The association between neighborhood socioeconomic disadvantage and high-risk injection behavior among people who inject drugs. Drug Alcohol Depend. 2017 Dec 8; 183:184-191. PMID: 29288913.

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Monica Lewin (Emotional Brain Institute) is the first author of this paper appearing in *Neuroscience*. The research, <u>described in this NYU</u> press release, was carried out by members of the Donald Wilson and Mariko Saito laboratories.

Lewin M, Ilina M, Betz J, Masiello K, Hui M, Wilson DA, Saito M. Developmental Ethanol-Induced Sleep Fragmentation, Behavioral Hyperactivity, Cognitive Impairment and Parvalbumin Cell Loss are Prevented by Lithium Co-treatment. Neuroscience. 2017 Nov 26; 369:269-277. PMID: 29183826.



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**Regina Sullivan** (Emotional Brain Institute) contributed this paper to a special issue of *Psychodynamic Psychiatry* on the neurobiology of attachment.

Sullivan RM. Attachment Figure's Regulation of Infant Brain and Behavior. Psychodyn Psychiatry. 2017 Winter;45(4):475-498. PMID: 29244623.



A total of seven papers from NKI's Schizophrenia Research group were published in a <u>special issue</u> of *Schizophrenia Research* focusing on mismatch negativity. Daniel Javitt coedited the issue.

## **JAMA Psychiatry**

**Helena Hansen** (Social Solutions & Services) coauthored these two Viewpoint pieces appearing in the February issue of *JAMA Psychiatry*, on the topic of structural competency training.

Metzl JM, Hansen H. Structural Competency and Psychiatry. JAMA Psychiatry. 2017 Dec 20. PMID: 29261822.

Hansen H, Braslow J, Rohrbaugh RM. From Cultural to Structural Competency-Training Psychiatry Residents to Act on Social Determinants of Health and Institutional Racism. JAMA Psychiatry. 2017 Dec 20. PMID: 29261827.

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Also in JAMA Psychiatry, Daniel Javitt (Schizophrenia Research) is the first author of a paper on the use of imaging biomarkers to improve drug development in schizophrenia. Joshua Kantrowitz and James Robinson are NKI coauthors. The paper is accompanied by an <u>invited</u> editorial, and is discussed in a <u>Columbia University</u> press release.

Javitt DC, Carter CS, Krystal JH, Kantrowitz JT, Girgis RR, Kegeles LS, Ragland JD, Maddock RJ, Lesh TA, Tanase C, Corlett PR, Rothman DL, Mason G, Qiu M, Robinson J, Potter WZ, Carlson M, Wall MM, Choo TH, Grinband J, Lieberman JA. Utility of Imaging-Based Biomarkers for Glutamate-Targeted Drug Development in Psychotic Disorders: A Randomized Clinical Trial. JAMA Psychiatry. 2018 Jan 1;75(1):11-19. PMID: 29167877.



**Michael Milham** (Biomedical Imaging & Neuromodulation) is the senior author of this *Scientific Data* paper describing the Child Mind Institute's Healthy Brain Network biobank of

multimodal data. **Russell Tobe** and **Xavier Castellanos** are NKI coauthors.

Alexander LM, Escalera J, Ai L, Andreotti C, Febre K, Mangone A, Vega-Potler N, Langer N, Alexander A, Kovacs M, Litke S, O'Hagan B, Andersen J, Bronstein B, Bui A, Bushey M, Butler H, Castagna V, Camacho N, Chan E, Citera D, Clucas J, Cohen S, Dufek S, Eaves M, Fradera B, Gardner J, Grant-Villegas N, Green G, Gregory C, Hart E, Harris S, Horton M, Kahn D, Kabotyanski K, Karmel B, Kelly SP, Kleinman K, Koo B, Kramer E, Lennon E, Lord C, Mantello G, Margolis A, Merikangas KR, Milham J, Minniti G, Neuhaus R, Levine A, Osman Y, Parra LC, Pugh KR, Racanello A, Restrepo A, Saltzman T, Septimus B, Tobe R, Waltz R, Williams A, Yeo A, Castellanos FX, Klein A, Paus T, Leventhal BL, Craddock RC, Koplewicz HS, Milham MP. An open resource for transdiagnostic research in pediatric mental health and learning disorders. Sci Data. 2017 Dec 19; 4:170181. PMID: 29257126.





The NIMH has redesigned the <u>Statistics section</u> of its website. The site now features interactive data visualization tools and sharing capabilities, as well as improved organization, navigation, and accessibility.

> DITZECTOTZ'S MESSAGE Joshua A. Gordon, M.D., Ph.D. Director of NIMH

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In his <u>latest Director's Message</u>, Dr. Gordon describes the principles that the NIMH has adopted for excellent science. These principles will facilitate comparisons between grant applications from across the diverse disciplines supported by the NIMH research portfolio.



**PubMed Central** (PMC), the free, full text repository of the National Library of Medicine, celebrated some milestones in 2017. Nearly half a million articles were made available for the public to access last year, and In October, the **one billionth** article of the year was retrieved. In a **recent blog post**, the NLM's Director wrote about PMC and some of its latest achievements.



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<u>ClinicalTrials.gov</u>, a database of clinical studies conducted around the world, has recently been updated to enhance its functionality. The search options on the home page and on the results page have been modified to help users find relevant studies and filter search results. A new in-context glossary feature has also been added. To read about these and other improvements to ClinicalTrials.gov, see this <u>NLM Technical Bulletin</u> <u>article</u>.



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Each year, *Nucleic Acids Research* publishes a database issue describing numerous databases spanning molecular biology. Among these are databases produced by the National Center for Biotechnology Information (NCBI), including GenBank, RefSeq, ClinVar, and CCDS. One article, "Database resources of the National Center for Biotechnology Information", summarizes NCBI's resources. *Nucleic Acids Research* also maintains a Molecular Biology Database Collection, organized by category.

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#### Interdepartmental Serious Mental Illness Coordinating Committee

In December, the **ISMICC** released its 2017 Report to Congress, titled *The Way Forward: Federal Action for a System That Works for All People Living with SMI and SED and Their Families and Caregivers.* The report presents the current status of federal activities and a summary of advances in the care and treatment of people with serious mental illnesses and serious emotional disturbances. The **Executive Summary** and the **full report** are both freely available to download.

#### **DEPARTMENT OF WONDER**

#### 2017 – Highlights in Science and Medicine

2018 is well underway, but it is worth taking a moment to consider some of the advances of the year that just concluded. Here are some year-end lists compiled by top agencies and publishers.



- <u>Clinical Advances</u>
- Promising Medical Advances
- Advances in Basic Research



<u>Research Highlights by Foundation</u>
<u>Grantees</u>



Breakthroughs of the Year



• Top Psychiatry Stories of 2017

The NKI librarian is always available to assist with literature searching, citation searching (Web of Science, Scopus), bibliographic reference management, and the like. When you have any information needs, or questions about available resources, don't hesitate to turn to us.

The library offers a comfortable, quiet space for reading, work, and small meetings. To use the library's Wi-Fi network, ask the library staff for the password.

You can link to the NKI Library's website from myNKI. The Library site includes quick links to the NYU Health Sciences Library and to the New York State Library, as well as links to NKI's own library resources (journal finder, online catalog, PsychiatryOnline, etc.). Remote access is available using NKI's VPN.

#### UPCOMING EVENTS AND SEMINARS

#### Center for Biomedical Imaging and Neuromodulation Science Series

Held on Mondays at 11 am

Mark Eldridge, PhD

Postdoctoral Fellow, NIH

#### Chemogenetic Interrogation of Reward Circuits in Monkey

March 5<sup>th</sup>

#### **Center for Dementia Research Seminar Series**

Held on Thursdays at 10 am

#### Ottavio Arancio, MD, PhD

Professor of Pathology and Cell Biology Columbia University Medical Center

#### Rearranging the puzzle: an alternative view on Alzheimer's disease

February 22<sup>nd</sup>

The New York State Office of Mental Health (OMH) regularly hosts an interactive video broadcast covering the latest research, technology, and treatment implementation in the fields of psychiatry and psychology. These programs are recorded, and the archived Statewide Grand Rounds programs can be viewed <u>on</u> <u>the OMH website</u>.

#### NKI ON THE ROAD



In addition to the 2017 American College of Neuropsychopharmacology (ACNP) annual meeting participants mentioned in the last issue, **Robert Smith, MD, PhD** (Neurochemistry) co-chaired a symposium on "Transcranial Electrical Stimulation for Improving Cognition in Schizophrenia: Preclinical and Clinical Insights". At the symposium, he also presented a paper from his tDCS study in China: "Effects of Transcranial Stimulation on Cognitive Function and Brain Functional Changes in Schizophrenia".



**Emily Stern, PhD** (Clinical Research) was the presenter at the January education meeting of **NAMI Rockland**. Her topic was "When Unwanted Thoughts Take over: Obsessive-compulsive disorder (OCD)"

#### NKI PUBLICATIONS UPDATE

Below is a list of references that have been added to the NKI publications database since the previous update. The full database contains over 5,700 items dating back to 1995, and can be searched from the <u>myNKI website</u>.

Alexander LM, Escalera J, Ai L, Andreotti C, Febre K, Mangone A, Vega-Potler N, Langer N, Alexander A, Kovacs M, Litke S, O'Hagan B, Andersen J, Bronstein B, Bui A, Bushey M, Butler H, Castagna V, Camacho N, Chan E, Citera D, Clucas J, Cohen S, Dufek S, Eaves M, Fradera B, Gardner J, Grant-Villegas N, Green G, Gregory C, Hart E, Harris S, Horton M, Kahn D, Kabotyanski K, Karmel B, Kelly SP, Kleinman K, Koo B, Kramer E, Lennon E, Lord C, Mantello G, Margolis A, Merikangas KR, Milham J, Minniti G, Neuhaus R, Levine A, Osman Y, Parra LC, Pugh KR, Racanello A, Restrepo A, Saltzman T, Septimus B, Tobe R, Waltz R, Williams A, Yeo A, Castellanos FX, Klein A, Paus T, Leventhal BL, Craddock RC, Koplewicz HS, Milham MP. An open resource for transdiagnostic research in pediatric mental health and learning disorders. Sci Data. 2017 Dec 19; 4:170181. PMID: 29257126.

Colibazzi T, Yang Z, Horga G, Chao-Gan Y, Corcoran CM, Klahr K, Brucato G, Girgis R, Abi-Dargham A, Milham MP, Peterson BS. Aberrant Temporal Connectivity in Persons at Clinical High Risk for Psychosis. Biol Psychiatry Cogn Neurosci Neuroimaging. 2017 Nov;2(8):696-705. PMID: 29202110.

DeCuir J, Lovasi GS, El-Sayed A, Lewis CF. The association between neighborhood socioeconomic disadvantage and high-risk injection behavior among people who inject drugs. Drug Alcohol Depend. 2017 Dec 8; 183:184-191. PMID: 29288913.

DeWitt SJ, Bradley KA, Lin N, Yu C, Gabbay V. A pilot resting-state functional connectivity study of the kynurenine pathway in adolescents with depression and healthy controls. J Affect Disord. 2017 Nov 20; 227:752-758. PMID: 29254065. Hansen H, Braslow J, Rohrbaugh RM. From Cultural to Structural Competency-Training Psychiatry Residents to Act on Social Determinants of Health and Institutional Racism. JAMA Psychiatry. 2017 Dec 20. PMID: 29261827.

Hatcher AE, Mendoza S, Hansen H. At the Expense of a Life: Race, Class, and the Meaning of Buprenorphine in Pharmaceuticalized "Care". Subst Use Misuse. 2018 Jan 28;53(2):301-310. PMID: 29161171.

Javitt DC, Carter CS, Krystal JH, Kantrowitz JT, Girgis RR, Kegeles LS, Ragland JD, Maddock RJ, Lesh TA, Tanase C, Corlett PR, Rothman DL, Mason G, Qiu M, Robinson J, Potter WZ, Carlson M, Wall MM, Choo TH, Grinband J, Lieberman JA. Utility of Imaging-Based Biomarkers for Glutamate-Targeted Drug Development in Psychotic Disorders: A Randomized Clinical Trial. JAMA Psychiatry. 2018 Jan 1;75(1):11-19. PMID: 29167877.

Jeanneteau F, Barrère C, Vos M, De Vries CJ, Rouillard C, Levesque D, Dromard Y, Moisan MP, Duric V, Franklin TC, Duman RS, Lewis DA, Ginsberg SD, Arango-Lievano M. The stress-induced transcription factor NR4A1 adjusts mitochondrial function and synapse number in prefrontal cortex. J Neurosci. 2018 Jan 2. PMID: 29295823.

Koyama MS, O'Connor D, Shehzad Z, Milham MP. Differential contributions of the middle frontal gyrus functional connectivity to literacy and numeracy. Sci Rep. 2017 Dec 13;7(1):17548. PMID: 29235506.

Köhler-Forsberg O, Sylvia L, Deckersbach T, Ostacher MJ, McInnis M, Iosifescu D, Bowden C, McElroy S, Calabrese J, Thase M, Shelton RC, Tohen M, Kocsis J, Friedman E, Ketter T, Nierenberg AA. Clinically relevant and simple immune system measure is related to symptom burden in bipolar disorder. Acta Neuropsychiatr. 2017 Dec 7:1-9. PMID: 29212563.

Lempert KM, McGuire JT, Hazeltine DB, Phelps EA, Kable JW. The effects of acute stress on the calibration of persistence. Neurobiol Stress. 2017 Nov 22; 8:1-9. PMID: 29214188. Lewin M, Ilina M, Betz J, Masiello K, Hui M, Wilson DA, Saito M. Developmental Ethanol-Induced Sleep Fragmentation, Behavioral Hyperactivity, Cognitive Impairment and Parvalbumin Cell Loss are Prevented by Lithium Co-treatment. Neuroscience. 2017 Nov 26; 369:269-277. PMID: 29183826.

Lieberman JA, Girgis RR, Brucato G, Moore H, Provenzano F, Kegeles L, Javitt D, Kantrowitz J, Wall MM, Corcoran CM, Schobel SA, Small SA. Hippocampal dysfunction in the pathophysiology of schizophrenia: a selective review and hypothesis for early detection and intervention. Mol Psychiatry. 2018 Jan 9. PMID: 29311665.

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Nuriel T, Peng KY, Ashok A, Dillman AA, Figueroa HY, Apuzzo J, Ambat J, Levy E, Cookson MR, Mathews PM, Duff KE. The Endosomal-Lysosomal Pathway Is Dysregulated by APOE4 Expression in Vivo. Front Neurosci. 2017 Dec 12; 11:702. PMID: 29311783.

Roberts M, Ashinoff BK, Castellanos FX, Carrasco M. When attention is intact in adults with ADHD. Psychon Bull Rev. 2017 Nov 27. PMID: 29181782.

Sayed S, Van Dam NT, Horn SR, Kautz MM, Parides M, Costi S, Collins KA, Iacoviello B, Iosifescu DV, Mathé AA, Southwick SM, Feder A, Charney DS, Murrough JW. A Randomized Dose-Ranging Study of Neuropeptide Y in Patients with Posttraumatic Stress Disorder. Int J Neuropsychopharmacol. 2018 Jan 1;21(1):3-11. PMID: 29186416.

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Sullivan RM. Attachment Figure's Regulation of Infant Brain and Behavior. Psychodyn Psychiatry. 2017 Winter;45(4):475-498. PMID: 29244623. Yanos PT, Stefancic A, Alexander MJ, Gonzales L, Harney-Delehanty B. Association between housing, personal capacity factors and community participation among persons with psychiatric disabilities. Psychiatry Res. 2017 Dec 5; 260:300-306. PMID: 29223799.

Goff D. Hippocampal atrophy, duration of untreated psychosis and molecular biomarkers during initial antipsychotic treatment of first episode psychosis. <u>Neuropsychopharmacology</u> <u>42[Suppl. 1]</u>, S108. 2017. [Abstract]

Hansen H. <u>Assisted Technologies of Social</u> <u>Reproduction: Pharmaceutical Prosthesis for</u> <u>Gender, Race, and Class in the White Opioid</u> <u>"Crisis"</u>. Contemporary Drug Problems 2017; 44(4):321-38.

Martinez A, Gaspar P, Hillyard S, Corcoran C, Stern Y, Javitt D. Differential deficits in early visual processing across neuropsychiatric populations: Implications for screening and intervention. <u>Neuropsychopharmacology 42[Suppl. 1]</u>, S438. 2017. [Abstract]

Pomara N, Bruno D, Nierenberg J, Zetterberg H, Blennow K, Heslegrave A, et al. Reduction in CSF STREM2, a biomarker of microglia activation, in elderly depressives. <u>Neuropsychopharmacology</u> <u>42[Suppl. 1]</u>, S409. 2017. [Abstract]

Sullivan R. Neurobiology of infant trauma: Specific categories of adversity produce diverse neurobiological signatures and outcome. <u>Neuropsychopharmacology 42[Suppl. 1]</u>, S50. 2017. [Abstract]

Yan CG, Yang Z, Colcombe SJ, Zuo XN, Milham MP. <u>Concordance among indices of intrinsic brain</u> <u>function: Insights from inter-individual variation</u> <u>and temporal dynamics</u>. Science Bulletin 2017; 62(23):1572-84.