News, Literature, and Events in Braingenethics

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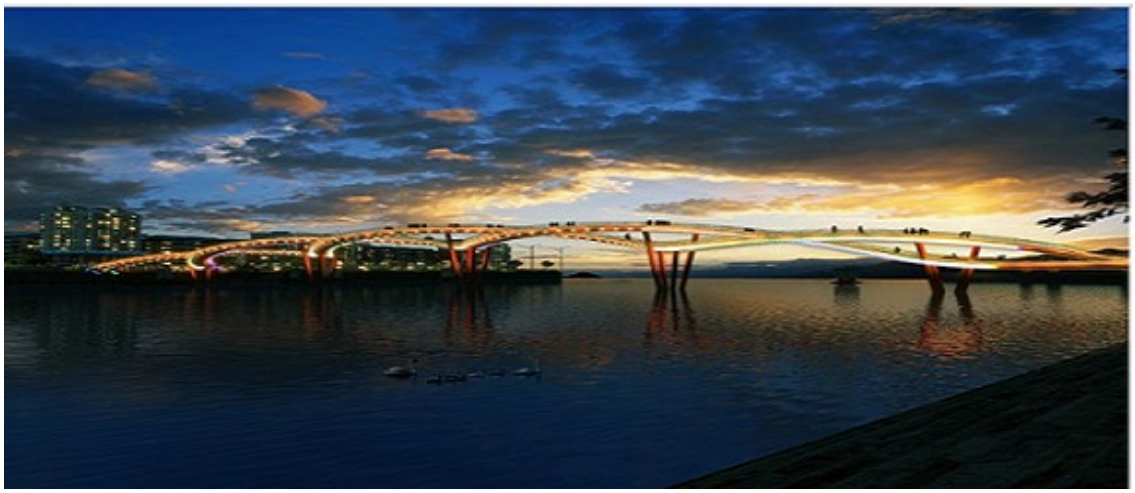

In the Literature

Psychiatric Genetics in Child Custody Proceedings: Ethical, Legal, and Social Issues

Maya Sabatello and Paul Appelbaum

While genetic tests cannot currently confirm a psychiatric diagnosis, as time goes on, psychiatric genetics will likely play a greater role in child custody proceedings. This paper examines possible scenarios for the introduction of this type of genetic information, and cautions against its unchecked use.

Judges' Views on Evidence of Genetic Contributions to Mental Disorders in Court

Colleen M. Berryessa

This preliminary analysis assesses how judges view the use of behavioral genetics of mental disorders in court and suggests

Shifts in Translational Research

What Happens When Underperforming Big Ideas in Research Become Entrenched?

Michael J. Joyner et al.

In the past several decades, genetic and genomic technologies have dominated clinical research. The authors illustrate this trend, and suggest how this focus has been problematic for health care and human health. They recommend that the NIH and other funding bodies evaluate the potential of translational or preclinical research, develop mechanisms for ending underperforming initiatives and

that some judges are skeptical of this evidence, but are largely open to its presentation.

Genetic Essentialist Biases, Stigma, and Lack of Mitigating Impact on Punishment Decisions

Colleen M. Berryessa

Responding to Scurich and Appelbaum, Berryessa identifies ways in which biases associated with genetic essentialist thinking might help to explain the lack of impact of genetic predispositions on punishment decisions.

Criminal Law, Neuroscience, and Voluntary Acts

Dennis Patterson

In this commentary on Maoz and Yaffe, Patterson suggests that the concept of "voluntary act" needs to be reassessed, as the voluntariness of an act cannot, as they suggest, be decided by scientific facts about the brain.

The Neuroscience of ADHD, the Paradigmatic Disorder of Self-Control

Robert Eme

In response to Maoz and Yaffe, Eme asserts that the future of work in the neuroscience of self-control will center on the most common neurodevelopmental disorder: attention deficit hyperactivity disorder (ADHD).

Informed Decision-Making About Prenatal cfDNA Screening: An Assessment of Written Materials

Marsha Michie et al.

As the introduction of prenatal cell-free DNA screening for genetic conditions exacerbates concerns about informed decision-making in clinical prenatal testing, this study examines what information patients have access to to inform their decision-making. The authors find significant variation in that information and offer recommended standards for

provide incentives for scientists to move on from research that is not delivering on its promise.

There's Such a Thing as Too Much Neuroscience

John C. Markowitz

Grants funded by the National Institute of Mental Health have become increasingly focused on translational neuroscience research. Such research is now "virtually required" as a component of mental health studies applying for funding, despite years of study still necessary for some technologies' clinical use. The author suggests that clinical research and DSM diagnoses offer immediate clinical utility and should receive greater recognition from funders, even if they don't contain neuroscience components.

In the Literature, cont.

Influence of Polygenic Risk Scores on the Association Between Infections and Schizophrenia

Michael E. Benros et al.

Several studies have suggested an important role of infections in the etiology of schizophrenia; however, shared genetic liability toward infections and

patient education and consent materials.

In the Media

One Family's Struggle with Microcephaly, the Birth Defect Now Linked to Zika

Marc Santora

Even before Zika emerged as a widely known public health risk, families were raising, and advocating on behalf of, children with microcephaly.

Can CRISPR-Cas9 Boost Intelligence?

Jim Kozubek

The accuracy with which CRISPR-Cas9 can edit genes, coupled with heightened understanding of the genetic components of intelligence, may one day make it possible to engineer augmented intelligence. But should we do so?

Philippa Levine Recommends the Best Books on Eugenics

Cal Flyn

In this Q&A, award-winning professor Philippa Levine cites some of her favorite books on eugenics, and discusses both the nuances of its history and its continued applications in modern reproductive decision-making.

Psychiatric Pharmacogenomics: How Close Are We?

Matthew E. Hirschtritt et al.

Pharmacogenomics, long the stuff of science fiction, is now a leading topic in the pursuit of precision medicine. While the field of oncology has been able to leverage genomic signatures to guide

schizophrenia could influence the association. This study investigated the possible effect of polygenic risk scores (PRSs) for schizophrenia on the association between infections and the risk of schizophrenia. It found that PRS and a history of infections have independent effects on the risk for schizophrenia, and the common genetic risk measured by PRS did not account for the association with infection in this sample.

GRIN2D Recurrent De Novo Dominant Mutation Causes a Severe Epileptic Encephalopathy Treatable with NMDA Receptor Channel Blockers

Dong Li et al.

Genetic mutations can cause various childhood epilepsy syndromes. In this study, a previously unrecognized missense mutation was found to contribute to seizure activity and resist conventional antiepileptic medications. These results guided a medication change in the treatment of two affected individuals, which resulted in mild to moderate improvement.

Biallelic Mutations in *TBCD*, Encoding the Tubulin Folding Cofactor D, Perturb Microtubule Dynamics and Cause Early-Onset Encephalopathy

Elisabetta Flex et al.

Microtubules are cytoskeletal elements that support several neuronal processes. This study identified mutations in the *TBDC* gene, which encodes for proteins necessary for the creation of the structure of microtubules. The defective *TBDC* gene caused phenotypes akin to neurodevelopmental and neurodegenerative disorders, including developmental delay, intellectual disability, and seizures. The authors suggest that *TBCD* functioning underlies microtubule production and, in turn, neuronal function

some treatments, psychiatric pharmacogenomics is in its infancy.

Genome-Wide Association Study of Loneliness Demonstrates a Role for Common Variation

Jia Hong Gao et al.

Loneliness is a complex biological trait that has been associated with numerous negative health outcomes. This study finds it to be a modestly heritable trait that has a highly polygenic genetic architecture, and notes that the coheritability between loneliness and neuroticism may reflect the role of negative affectivity that is common to both traits.

DNA Methylation Signatures of Early Childhood Malnutrition Associated with Impairments in Attention and Cognition

Cyril J. Peter et al.

This study explored molecular signatures after childhood malnutrition, including the potential for intergenerational transmission. It found a number of genomic regions where the epigenetic effects of early childhood malnutrition could be detected, but noted a limited potential for intergenerational transmission.

BRG1 in the Nucleus Accumbens Regulates Cocaine-Seeking Behavior

Zi-Jun Wang et al.

Neurobiological adaptations are thought to contribute to compulsive drug-seeking behavior. This study investigated a possible interaction of an enzyme, BRG1, with the transcription factor SMAD3 in response to cocaine exposure in rats. It found that BRG1 is a key mediator of cocaine-seeking behaviors after a period of withdrawal.

A Test-Replicate Approach to Candidate Gene Research on Addiction and Externalizing Disorders: A Collaboration

and survival in developing brains.

De Novo Mutations in *CHD4*, an ATP-Dependent Chromatin Remodeler Gene, Cause an Intellectual Disability Syndrome with Distinctive Dysmorphisms

Karin Weiss et al.

Using whole-exome sequencing and web-based gene matching, Weiss et al. identified five individuals with de novo missense substitutions in *CHD4*, a DNA-binding protein involved in gene transcription, DNA repair, and cell cycle progressions. The individuals exhibit overlapping phenotypes, including developmental delay, intellectual disability, hearing loss, and macrocephaly. The authors suggest that *CHD4* contributes to human development and Mendelian disorders driven by chromatin remodeling and modification.

Mutations in *MBOAT7*, Encoding Lysophosphatidylinositol Acyltransferase I, Lead to Intellectual Disability Accompanied by Epilepsy and Autistic Features

Anide Johansen et al.

The risk of epilepsy among individuals with intellectual disability is approximately ten times that of the general population. This study suggests a role for AA-containing phosphatidylinositols (major lipids in the mammalian brain) in the development of intellectual disability accompanied by epilepsy and autistic features.

NAXE Mutations Disrupt the Cellular NAD(P)HX Repair System and Cause a Lethal Neurometabolic Disorder of Early Childhood

Laura S. Kremer et al.

This study deployed whole-exome sequencing datasets to identify the molecular basis of a disorder of metabolite repair. These findings may be of clinical

Across Five Longitudinal Studies

Diana R. Samek et al.

This study presents results from a collaboration across five longitudinal studies seeking to test and replicate models of gene-environment interplay in the development of substance use and externalizing disorders. One significant main effect was found in the test sample, but it was not replicated.

Chromosome Conformation Elucidates Regulatory Relationships in Developing Human Brain

Hyejung Won et al.

The 3D organization of chromosomes during human brain development and its role in regulating gene networks dysregulated in neurodevelopmental disorders, such as autism or schizophrenia, are unknown. This analysis, which identified hundreds of genes that interact with genetic enhancers (short sequences of DNA involved in the process of gene transcription) provides a framework for understanding the effect of noncoding regulatory elements on human brain development, and highlights novel mechanisms underlying neuropsychiatric disorders.

Reduced Sleep Spindles in Schizophrenia: A Treatable Endophenotype that Links Risk Genes to Impaired Cognition?

Dara S. Manoach et al.

Abnormal sleep is a common feature of schizophrenia.This study examines sleep spindles, a feature of sleep thought to enhance memory consolidation, and shows that they can be pharmacologically enhanced and serve as a novel treatment biomarker. They are highly heritable, and should form the basis of future genetic study.

use during differential diagnosis.

TMEM231 Gene Conversion Associated with Joubert and Meckel-Gruber Syndromes in the Same Family

Dino Maglic et al.

Joubert and Meckel-Gruber syndromes are genetically heterogeneous disorders that share some symptoms and underlying genes. Using whole exome sequencing, Maglic et al. identified the loss of exon 4 in the *TMEM231* gene in a family with several children with symptoms of JS and MGS. The authors believe that the spectrum of JS and MGS phenotypes resulted from a gene conversion (which was responsible for the loss of the exon) in combination with missense mutations.

Down-Regulation of *SIRT1* Gene Expression in Major Depressive Disorder

Xiong-Jian Luo & Chen Zhang

While major depressive disorder (MDD) is heritable, its genetic underpinnings are largely unknown. The authors of this letter to the editor outline their findings that *SIRT1* expression is significantly down-regulated in MDD patients, but note that MDD is most likely also influenced by many yet-undiscovered loci.

The Role of *PIEZO2* in Human Mechanosensation

Alexander T. Chesler

This study implicates the stretch-gated ion channel *PIEZO2* in mechanosensation, which involves the sense of touch and the ability to detect stimuli related to the body's relative position and motion.

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Upcoming Events

November Seminar on Ethical, Legal and Social Implications of Genetics

Monday, November 7th, 2016, 12:00 pm, Sergievsky Center Room 19-201, Columbia University Medical Center

This month's speaker is Dr. Barbara Bernhardt, a Clinical Professor of Medicine and Genetic Counselor at the University of Pennsylvania's Deptartment of Medicine. Dr. Bernhardt's talk is titled "Receiving Uncertain Genomic Test Result During Pregnancy: Decision-Making and the Aftermath."

Webinar: Methods for Validating a Gene Editing Approach to Treating Brain Disease with Zinc Fingers, TALEs, and CRISPR/Cas9

Wednesday, November 9, 2016, 11:00 am EST (8:00 am PST/5:00 pm CET)

Sponsored by Wiley, this webinar will feature Dr. David Segal, a Professor of Biochemistry and Molecular Medicine in the UC-Davis Genome Center, and Dr. Jun Park, lead Applications Scientist at MilliporeSigma. Presenters will discuss methods of modifying genetic and epigenetic information through gene editing, delivering gene editing tools into the brains of live animals, using quantitative Western blotting as a validation tool, and the challenges of using gene editing in the brain.

2017 Genomics and Society: Expanding the ELSI Universe (The 4th ELSI Congress)

June 5, 2017, The Jackson Laboratory for Genomic Medicine and UConn Health, Farmington, CT

This is the latest in a series of major conferences for ELSI researchers and others interested in the ethical, legal, and social implications of genomic research. **Abstract Submissions due December 1st**

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