News, Literature, and Events in Braingenethics

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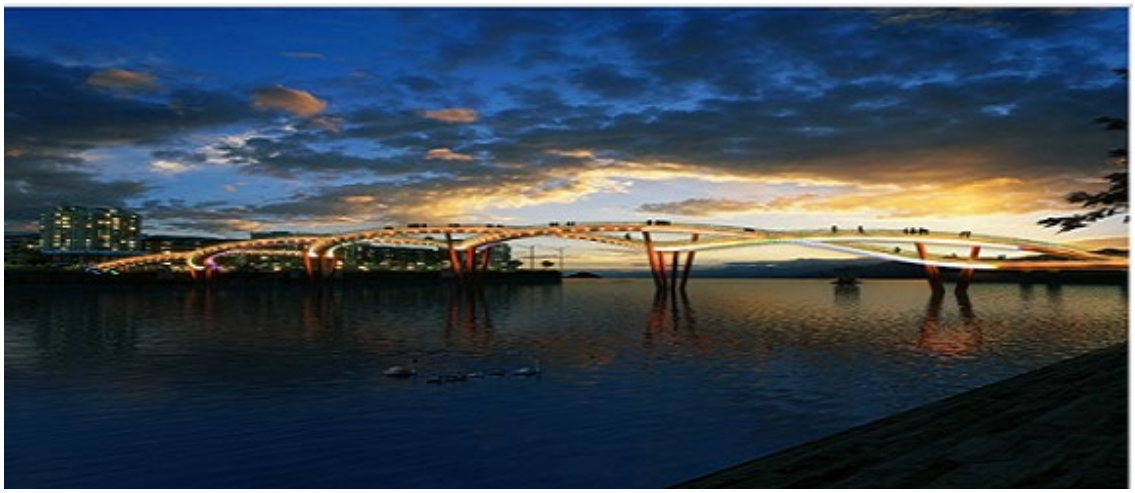

In the Literature

A Genomically Informed Education System? Challenges for Behavioral Genetics

Maya Sabatello

The growth of genetic knowledge raises the concern that behavioral, including psychiatric genetic data, would be increasingly misused outside the clinical context, such as educational settings. Indeed, there are ongoing calls to endorse a "personalized education" model that would tailor educational interventions to children's behavioral and psychiatric genetic makeup. This article explores the justifications for, and prospects and pitfalls of such endeavors.

Genetic Privacy, Disease Prevention, and the Principle of Rescue

In the Media

Do You Want the Police Snooping in Your DNA?

Wendy Chung et al.

CEER faculty, including Director Paul Appelbaum, write about the recent case of the Golden State Killer, discussing evolving ways that law enforcement is using genetic data to identify suspects, and the consequent risks to the privacy of genetic data.

With Tantalizing Early Results, Sarepta's Gene Therapy for Duchenne Raises Hopes for 'Real Change'

Adam Feurstein

An experimental gene therapy for

Madison K. Kilbride
Suppose that you have deeply personal information that you do not want to share, but, that this information could help others, perhaps even saving their lives. With the increasing prevalence of genetic testing, more and more people are finding themselves in this situation. This paper explores the duty to share one's genetic results as grounded in the principle of rescue—the idea that one ought to prevent, reduce, or mitigate the risk of harm to another person when the expected harm is serious and the cost or risk to oneself is sufficiently moderate.

Return of Research Results to Study Participants: Uncharted and Untested
Charlene A. Wong et al.
Research data may be of great utility to study participants and their clinicians in understanding the health of patients who participate in research. With increasing digitization and data availability, researchers, clinicians, developers, and patients encounter the issue of how to consume, analyze, and make sense of those data. The return of individual results in the context of research studies provides a useful, structured environment to develop an empirical framework, and lessons learned may be applicable to other cases of health information consumerism.

Genome-wide Association Meta-analysis in 269,867 Individuals Identifies New Genetic and Functional Links to Intelligence
Jeanne E. Savage et al.
This is a large-scale genetic association study of intelligence identifying 205 associated genomic loci (190 new) and 1,016 genes (939 new). Associated genes are strongly expressed in the brain, specifically in striatal medium spiny neurons and hippocampal pyramidal

Duchenne muscular dystrophy produced exciting results in patients with the disease, according to preliminary clinical trial data.

Rapid Genome Sequencing Could Revolutionize Health Care for Acutely Ill Babies
Sarah Elizabeth Richards
Researchers at the Rady Genomics Institute in California found that rapid genome sequencing is cost-effective and diagnostically superior to other methods for the diagnosis of acutely ill newborns. The Rady Institute is a part of the NSIGHT program, a national study investigating the use of sequencing in various newborn contexts. The Hastings Center works with the NSIGHT team at the University of California San Francisco to evaluate the ethical issues of sequencing in newborns.

F.D.A. Panel Recommends Approval of Cannabis-based Drug for Epilepsy
Shelia Kaplan
A Food and Drug Administration advisory panel unanimously recommended approval of an epilepsy medication made with cannabidiol (CBD), one of the chemical compounds found in marijuana (not the one that causes intoxication).

Finding New Treatments for Parkinson's and Alzheimer's Shouldn't Be Up to Pharma Alone
Allan Hugh Cole Jr.
Pharmaceutical giants forming venture capital groups is an innovative twist in drug development. But new approaches

neurons. The study suggests protective effects of intelligence for Alzheimer's disease and ADHD and bidirectional causation with pleiotropic effects for schizophrenia.

Meta-analysis of Genome-wide Association Studies for Neuroticism in 449,484 individuals Identifies Novel Genetic Loci and Pathways

Mats Nagel et al.

This large GWAS meta-analysis (n = 449,484) of neuroticism identified 136 independent genome-wide significant loci (124 new at the time of analysis), which implicate 599 genes. The study finds that that neuroticism's genetic signal partly originates in two genetically distinguishable subclusters ('depressed affect' and 'worry'), suggesting distinct causal mechanisms for subtypes of individuals. Analysis showed correlations between neuroticism and multiple psychiatric traits.

A Molecular Signature for Social Isolation Identified in the Brain

Noga Zilkha & Tali Kimchi

Extended social isolation causes debilitating effects in social mammals such as humans. A study of socially isolated mice shows that the gene Tac2 is upregulated throughout the brains after long periods of isolation. Tac's increased expression causes massive behavioral changes, such as enhanced aggression (regulated by Tac in the hypothalamus), and acute and persistent stress responses (regulated by Tac in the amygdala).

they shouldn't come just from the pharma industry. Personal sacrifice, political will, and a shared commitment to the public good must also play roles.

Alzheimer's: Rethinking the 'One-Size-Fits-All' Approach

Judy George

A key theme at the 2018 Alzheimer's Disease Research Summit was precision medicine in Alzheimer's disease, with a particular focus on the need to differentiate patients based on genetics, environmental exposure to toxins, and clinical history.

23andMe: Feeling 'Hangry' May Be in Our Genes

Alexa Lardieri

A 23andMe survey and genome-wide association study found that two sets of genetic variants may predispose people to feeling angry or irritable when hungry. One of the genes is associated with schizophrenia, depression, epilepsy and multiple sclerosis, the other is associated with subjective well-being, irritability and neuroticism.

The Weird, Ever-Evolving Story of DNA

Nathaniel Comfort

Carl Zimmer's new book, *She Has Her Mother's Laugh*, forces readers to reconsider what they think they know about genetics and heredity.

Trio of Genes Supercharged Human Brain Evolution

Elizabeth Pennisi

Three nearly identical genes could help explain how our brains evolved from early human ancestors, and

[Analysis of Shared Heritability in Common Disorders of the Brain]

The Brainstorm Consortium

This study of almost 900,000 people by an international consortium of hundreds of scientists assembled genome-wide association study data for 25 psychiatric and neurological disorders. The study found that 10 mental illnesses share genetic variants that contribute to the risk of their development.

More in the Media, quoting CEER Deputy Director Ruth Ottman: Common Gene Variants Found Among Psychiatric Disorders

[Nanoparticle Delivery of CRISPR into the Brain Rescues a Mouse Model of Fragile X Syndrome from Exaggerated Repetitive Behaviours]

Bumwhee Lee et al.

A University of Texas, San Antonio and University of California, Berkeley team CRISPR-edited a causal gene for fragile X syndrome in a mouse model, and effectively reduced repetitive behaviors that are symptomatic of the disorder. Researchers believe this gene editing technique could be used other neurological disorders, such as epilepsy, if the gene target is known.

[Multiscale Analysis of Independent Alzheimer's Cohorts Finds Disruption of

likely play a role in neurological disorders.

More In the Literature

[Multi-gene Panel Testing in Korean Patients with Common Genetic Generalized Epilepsy Syndromes]

Cha Gon Lee et al.

This multi-gene sequencing study analyzed potential candidate or susceptibility genes for common genetic generalized epilepsy syndromes. It identified candidate genetic variants in about a quarter of patients and an average of 2.8 variants was identified in each patient. The results reinforced the polygenic disorder with very high locus and allelic heterogeneity.

[Identification of Rare de novo Epigenetic Variations in Congenital Disorders]

Mafalda Barbosa et al.

By comparing DNA methylation profiles from 489 individuals with neurodevelopmental disorders and congenital anomalies (ND-CAs) against 1534 controls, this study identified de novo epigenetic variations that often have an impact on gene expression comparable to loss-of-function mutations. The research suggests that epivariations contribute to the pathogenesis of some patients with unexplained ND–CAs.

[A Homozygous Loss-of-function CAMK2A Mutation Causes Growth Delay, Frequent Seizures and Severe Intellectual Disability]

Poh Hui Chia et al.

This paper describes a new recessive

Molecular, Genetic, and Clinical Networks by Human Herpesvirus

Ben Readhead et al.

This study constructed multiscale networks of the late-onset Alzheimer's Disease (AD)-associated virome, to understand whether pathogenic microbes might contribute to the onset and progression of Alzheimer's disease (AD). Researchers observed increases in two strains of human herpesvirus from subjects with AD compared with controls. The viruses may play a role in regulatory genetic networks that lead to the disease.

APOE4 Causes Widespread Molecular and Cellular Alterations Associated with Alzheimer's Disease Phenotypes in Human iPSC-Derived Brain Cell Types

Yuan-Ta Lin et al.

Using CRISPR/Cas9 and induced pluripotent stem cells (iPSCs), researchers observed APOE4's effects on human brain cell types. In comparison to APOE3, APOE4 causes molecular and cellular alterations in synaptic function in neurons, lipid metabolism in astocytes, and immune response in microglia-like cells. Consistently, converting APOE4 to APOE3 in brain cell types was sufficient to attenuate multiple AD-related pathologies.

Fast-Evolving Human-Specific Neural Enhancers Are Associated with Aging-Related Diseases

Han Chen et al.

This study analyzed neural enhancer evolution in primates to investigate the relationships between aging-related diseases and enhancers acquired after the human-chimpanzee divergence. Researchers used CRISPR/Cas9 to validate an enhancer on a regulator known to be a transcriptional suppressor of Alzheimer disease. The study suggests that adaptive molecular changes in human macroevolution may introduce neurodevelopmental syndrome with global developmental delay, seizures, and intellectual disability. This study used linkage analysis and exome sequencing to find that the disease maps to chromosome 5q31.1-q34 and is caused by a biallelic missense germline mutation in Calcium/calmodulin-dependent protein kinase II (CAMK2), which is known to play fundamental roles in synaptic plasticity that underlies learning and memory.

Genetic Testing to Reunite Immigrant Families Raises Issues of Privacy and Consent

Karen Weintraub

More than 2,000 children have been separated from their parents at the US border as a result of the White House's new "zero tolerance" policy, and immigration agencies seem to have no clear plan for reuniting them. In the midst of the crisis, consumer DNA companies like 23andMe and MyHeritage are offering their services as an unlikely solution. Bioethicists and lawyers discuss the ethical issues raised by this proposal.

Leading Immigrant Aid Group Says No Thanks to 23andMe Offer to Help Reunite Detained Families ·

Sara Hossaini

In light of privacy concerns, leading immigrant aid group RAICES Texas denies 23andMe's offer to provide genetic testing to reunite immigrant families.

Assessment of a Targeted Gene Panel for Identification of Genes Associated with Movement Disorders

Solveig Montaut et al.

vulnerabilities to disease development in modern populations, and explain the evolutionary origins of aging-related diseases such as Alzheimer's and cancers.

Convergence of Placenta Biology and Genetic Risk for Schizophrenia

Gianluca Ursini et al.

This study suggests that the intra-uterine environment modulates the association of schizophrenia with genomic risk. In contrast to prior studies, this research found that many genes associated with risk for schizophrenia appear to alter early brain development *indirectly*, by influencing the health of the placenta. The research concluded that these significant genetic variants associated with schizophrenia are switched on in the placenta during complicated pregnancies and signal a placenta under duress.

Genomic Dissection of Bipolar Disorder and Schizophrenia, Including 28 Subphenotypes

Bipolar Disorder and Schizophrenia Working Group of Psychiatric Genomics Consortium

This study identified 114 genome-wide significant loci implicating synaptic and neuronal pathways shared between Schizophrenia (SCZ) and bipolar disorder (BD). Comparing SCZ to BD identified four genomic regions as contributing to differences in biology between the disorders. The study found specific loci that distinguish between BD and SCZ and identify polygenic components underlying multiple symptom dimensions.

Exon Array Biomarkers for the Differential Diagnosis of Schizophrenia and Bipolar Disorder

Marquis P. Vawter et al.

This study developed potential blood-based biomarker tests for diagnosing and differentiating schizophrenia (SZ), bipolar

This study successfully created a targeted sequencing gene panel to identify genes associated with movement disorders. The panel was efficient and provided a cost-effective diagnostic alternative to whole-exome and whole-genome sequencing.

Longitudinal Analysis of Impulse Control Disorders in Parkinson Disease

Jean-Christophe Corvol et al.

This longitudinal study of patients with Parkinson's Disease tracked the correlation between impulse control disorders (ICDs) and dopamine agonist (DA) treatment. Both increasing duration and dose of DAs were strongly associated with ICDs. ICDs progressively resolved after DA discontinuation.

Bacteriophages: Are They an Overlooked Driver of Parkinson's Disease?

George Tetz et al.

This poster from the American Society for Microbiology Annual Conference links bacteriophages to Parkinson's disease. Significant shifts can be observed in gut phagobiota of PD patients which can be considered to be a disease hallmark or trigger. The study suggests future research into the connection between PD and bacteriophages.

DNA Methylation as a Mediator of HLA-DRB1*15:01 and a Protective Variant in Multiple Sclerosis

Lara Kular et al.

The human leukocyte antigen (HLA) haplotype DRB1*15:01 is the major risk factor for multiple sclerosis (MS). This meta-analysis of 14,259 cases and 171,347 controls confirms that HLA variants confer risk for MS from DRB1*15:01 and also identifies a protective variant after conditioning for all MS-associated variants in the region.

Quantifying the Impact of Rare and Ultra-rare Coding Variation Across the

disorder type I (BD), and normal control (NC) subjects using mRNA gene expression signatures. The study found stable trait gene panel markers for lifelong psychiatric disorders that may have diagnostic utility in younger undiagnosed subjects where there is a critical unmet need.

[De novo Variants in Neurodevelopmental Disorders with Epilepsy]

Henrike O. Heyne et al.

Epilepsy is a frequent feature of neurodevelopmental disorders (NDDs), but little is known about genetic differences between NDDs with and without epilepsy. This study identified 33 genes with a significant excess of de novo variants (DNV) in the subset of individuals with NDDs with epilepsy. Missense DNVs, DNVs in specific genes, age of recruitment, and severity of intellectual disability were associated with NDDs with epilepsy, in comparison to NDDs without epilepsy.

[Phenotypic Spectrum]

Andrea Ganna

This whole-exome sequencing study investigated the impact of rare protein-truncating variants on 13 quantitative traits and 10 diseases. Protein-truncating variants in genes intolerant to this class of mutations increased risk of autism, schizophrenia, bipolar disorder, intellectual disability, and ADHD.

[A Molecular Mechanism for Choosing Alcohol Over an Alternative Reward]

Eric Augier et al.

This mouse study on addiction found that the GABA transporter GAT-3 was selectively decreased within the amygdala of alcohol-choosing mice, whereas a knockdown of this transcript reversed choice preference of mice that originally chose a sweet solution over alcohol. GAT-3 expression was selectively decreased in the central amygdala of alcohol-dependent people compared to those who died of unrelated causes. Impaired GABA within the amygdala contributes to alcohol addiction and may offer targets for new pharmacotherapies.

Looking for the Psychosocial Impacts of Genomic Information

Watch the archive from our February conference here.

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