News, Literature, and Events in Braingenethics

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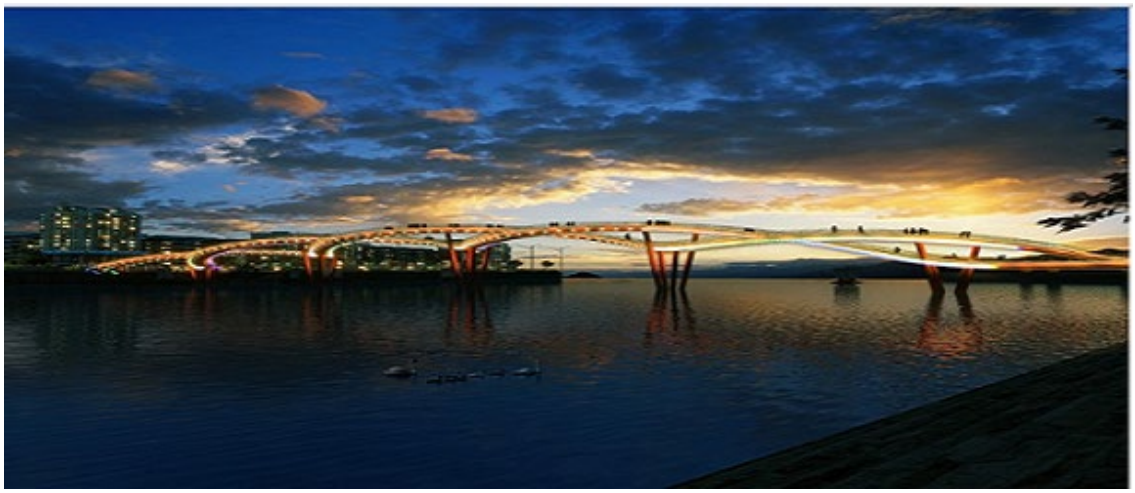
Braingenethics Update

Vol. 5, No. 9
December 2018
braingenethics.cumc.columbia.edu/



The next Braingenethics Update (Vol. 6, No. 1) will appear in late January 2019.

In the Literature

Ethical Issues in Susceptibility Genetic Testing for Late-Onset Neurodegenerative Diseases
Amaranta Manrique de Lara et al.
Ethical issues in genetic testing for Alzheimer's and Parkinson's include informed consent, disclosure of findings, screening, privacy, stigma, and genetic discrimination. Appropriate counseling is crucially important for the ethical use of genetic testing.

Learning One's Genetic Risk Changes Physiology Independent of Actual Genetic Risk

In the Media

What Happens When You're Convinced You Have Bad Genes
Sarah Zhang
Independent of actual genetic data, false genetic information indicating elevated risk for obesity in two genes related to aerobic fitness and hunger caused study subjects to exercise less intensely and eat more, with physiological correlates like oxygen and hunger-hormone levels matching self-reporting.

Studying Personal Genomics: Expanding the Pool

Bradley P. Turnwald et al.
Receiving information about genetic susceptibility to obesity, regardless of veracity, alters physiology and related behaviors in a self-fulfilling manner, in some areas proving more impactful than actual genetic susceptibility.

Perceived Unfair Treatment by Police, Race, and Telomere Length: A Nashville Community-based Sample of Black and White Men
Michael J. McFarland et al.
Shortened telomere length correlates with unfair treatment by police, whether experienced personally or indirectly through one's family or friends, offering a plausible physiological mechanism for poor health outcomes in minority populations.

ASHG Denounces Attempts to Link Genetics and Racial Supremacy
ASHG Board of Directors
The American Society for Human Genetics denounces the mis-use of human genetic research for racist ends.

Comprehensive Functional Genomic Resource and Integrative Model for the Human Brain
Daifeng Wang et al.
A multi-scale brain resource from the PsychENCODE Consortium links multiple data types to construct a comprehensive multi-scale database of the human brain. It embeds a derived gene regulatory network into a deep-learning model, which improves disease prediction by about six-fold versus polygenic risk scores alone.

Expression Quantitative Trait Loci in the Developing Human Brain and Their Enrichment in Neuropsychiatric Disorders
Heath E. O'Brien et al.
O'Brien and colleagues present the first

Robert C. Green
The PeopleSeq Consortium plans to explore the implications of genomic risk through a longitudinal study that tracks the actions and outcomes of healthy adults who have chosen to be sequenced, with an emphasis on recruiting a more ancestrally diverse sample.

Sigrid Johnson Was Black. A DNA Test Said She Wasn't.
Ruth Padawer
The surge in popularity of direct-to-consumer genetic testing means that more and more people are unearthing long-buried connections and surprises in their ancestry.

I Was Raised as a Native American. Then a DNA Test Rocked My Identity
Sequoya Yiaueki
The author experiences difficulties coming to terms with learning that the Indian heritage his father told him he inherited was fabricated.

Woman Who Inherited Fatal Illness to Sue Doctors in Groundbreaking Case
Robin McKie
In a case with major implications for how and when providers disclose genetic information, a London woman who discovered – after giving birth – that her father carried the gene for Huntington's disease is suing the hospital for non-disclosure of results.

Mapping the Brain's Genetic Landscape
Benedict Carey
A consortium of researchers has produced the most richly detailed

genome-wide expression quantitative trait loci (eQTL) mapping specifically in fetal brains. They provide evidence that these confer risk for certain neuropsychiatric disorders and identify gene expression changes that potentially mediate susceptibility to these conditions.

Polygenic Risk Score for Schizophrenia Is More Strongly Associated with Ancestry Than with Schizophrenia
David Curtis
Distributions of polygenic risk scores for schizophrenia are dramatically different for European and African ancestries; this suggests validity only within ancestral populations and raises ethical issues regarding clinical utility and unequal health provision.

Schizophrenia Polygenic Risk Score as a Predictor of Antipsychotic Efficacy in First-Episode Psychosis
Jian-Ping Zhang et al.
Patients with higher PRSs for schizophrenia tend to have less improvement with antipsychotic drug treatment following first-episode psychosis.

Effect of Damaging Rare Mutations in Synapse-Related Gene Sets on Response to Short-term Antipsychotic Medication in Chinese Patients with Schizophrenia
Qiang Wang et al.
Whole-exome sequencing was used to identify variants in two gene sets in the glutaminergic system that predict poor response to anti-psychotics for first-episode schizophrenia in a Han Chinese sample.

Biobank-Wide Association Scan Identifies Risk Factors for Late-onset Alzheimer's Disease and Endophenotypes
Donghui Yan et al.

model of the brain's genetic landscape to date—one that incorporates not only genes but also gene regulators, cellular data, and developmental information across the human life span, offering new possibilities for identifying genetic roots of psychiatric disorders.

Wired That Way: Genes Do Shape Behaviors but It's Complicated
Kevin Mitchell
Recent research in brain development and genetics illustrate just how complicated the relationship between genes, brains, and psychological traits truly is.

Genetic Link to Cerebral Palsy May be More Common Than Thought, Suggests Large Study Presented at NSGC Meeting
NSGC Blog
Up to 1 in 3 people with cerebral palsy may have the condition due to an underlying genetic cause, suggests a study of more than 1,300 people with cerebral palsy.

Team Co-Led By UCSD Finds Genetic Link to Autism in Children
Debbie L. Sklar
Gene expression in white blood cells is linked specifically to poor language development in Autistic toddlers.

A Vast Study Seeks to Understand the Genetic Underpinnings of ADHD
The Economist
A genome-wide association study of more than 20,000 people of European ancestry diagnosed with ADHD has identified 12 loci associated with the disorder. Evidence supports the clinical

A new, open-source toolset, BADGERS, has been introduced to identify associations between a disease and polygenic risk scores using GWAS summary data. In this study, BADGERS was used to identify 48-trait PRSs that in turn are significantly associated with Alzheimer's disease.

Dissecting the Genetic Relationship between Cardiovascular Risk Factors and Alzheimer's Disease
Iris J. Broce et al.
Beyond APOE, the authors identify a subset of cardiovascular-associated genes that strongly increase the risk for Alzheimer's disease, suggesting that cardiovascular biology is integral to the development of clinical AD in a subset of individuals.

APOE Genotypes in Lebanon: Distribution and Association with Hypercholesterolemia and Alzheimer's Disease
Said El Shamieh et al.
The authors present findings for the distribution of APOE genotypes in the Lebanese population and show that in contrast to lipid profile, the E4 APOE allele correlates with Alzheimer's disease.

Somatic APP Gene Recombination in Alzheimer's Disease and Normal Neurons
Ming-Hsiang Lee et al.
Neuronal gene recombination may allow "recording" of neural activity for selective "playback" of preferred gene variants whose expression bypasses splicing; this has implications for cellular diversity, learning and memory, plasticity, and diseases of the human brain.

The Intellectual Disability Gene PQBP1 Rescues Alzheimer's Disease Pathology
Hikari Tanaka et al.

assumption that ADHD is an extreme expression of continuous heritable traits.

FDA Takes New Action to Advance the Development of Reliable and Beneficial Genetic Tests That Can Improve Patient Care
FDA News Release
The FDA is recognizing the open ClinGen Expert Curated Human Genetic Data bank as a source of valid scientific evidence for genetic variant information that can be used to support clinical validity in premarket submissions. This recognition will allow developers of genetic tests to rely on the information available in the database to support the validity of their tests, instead of having to generate the information on their own.

Cracking the Genetic Code of Bipolar Disorder
Australian Genetics of Bipolar Disorder Study Press Release
Australian researchers are seeking 5,000 adults who have been treated for bipolar disorder to volunteer for the world's largest genetic investigation of bipolar.

Drugs developed to remove beta-amyloid plaque are ineffective at reversing functional losses in Alzheimer's disease, leading researchers to look for precursors to plaque formation. Here, researchers identified intracellular markers of Alzheimer's disease that precede the formation of beta-amyloid plaque currently used for diagnosis. Using a virus vector to restore a gene whose impaired expression is associated with intellectual disability, and which is affected by Alzheimer's-linked phosphorylation, recovers synaptic structures and cognitive function in Alzheimer's model mice.

Sibling Recurrence Risk and Cross-aggregation of Attention-Deficit/Hyperactivity Disorder and Autism Spectrum Disorder

Meghan Miller et al.

Later-born siblings of children on the Autism Spectrum appear to be at elevated risk for both Autism and ADHD, with the same effect documented for later-born siblings of children diagnosed with ADHD. This has implications for etiological overlap and clinical monitoring of both.

Discovery of the First Genome-Wide Significant Risk Loci for Attention Deficit/Hyperactivity Disorder

Ditte Demontis et al.

A genome-wide association study reveals the first 12 loci identified with ADHD.

Progress in Brain Research: Genetic Models and Molecular Pathways Underlying Autism Spectrum Disorder

Ed. Anantha Shekhar

Chapter 1 – Overview of Genetic Models of Autism Spectrum Disorders

Jheel Patel et al.

The authors discuss a subset of genetic models of Autism Spectrum Disorder (ASD), focusing on models that have been widely studied and strongly linked to ASD.

Chapter 4 – From Bedside to Bench and Back: Translating ASD Models

Hayley P. Drozd et al.

Biomarker work is expanding researchers' understanding of possible mechanisms of ASD through measures of behavior, genetics, imaging modalities, and serum markers. These biomarkers could help to subclassify patients with ASD in order to better target treatments.

Chapter 5 – Studying Child Development in Genetic Models of

Analyses of three replication studies support these findings while highlighting study-specific differences on genetic overlap with educational attainment.

Use of Polygenic Risk Scores of Nicotine Metabolism in Predicting Smoking Behaviors

Li-Shiun Chen et al.

Polygenic risk scores for nicotine metabolism correlate with nicotine metabolism biomarkers but did not predict smoking quantity or cessation in this study.

Understanding the Role of Bitter Taste Perception in Coffee, Tea and Alcohol Consumption through Mendelian Randomization

Jue-Sheng Ong et al.

Across three genes associated with bitterness perception, increased caffeine bitterness perception was correlated with higher coffee consumption, and alcohol consumption was inversely correlated with a gene regulating perception of propylthiouracil. The study results demonstrate a causal association between bitter perception and intake of coffee, tea, and alcohol.

ASD

Shruti Garg and Jonathan Green

This chapter approaches the early development of ASD through a comparative study of key monogenic syndromic ASD models in humans.

More In the Literature

Epilepsy Control with Carbamazepine Monotherapy from a Genetic Perspective

Shakir Ullah et al.

Heterozygous variants of the MTHFR gene are associated with poor seizure control in patients of Pakhtun ancestry despite therapeutic levels of carbamazepine in plasma.

NFIB Haploinsufficiency Is Associated with Intellectual Disability and Macrocephaly

Ina Schanze et al.

Based on study of a cohort with intellectual disabilities and subsequent comparison with mice knockout models, authors conclude that inheriting only one functional copy of NFIB, a transcription factor from the nuclear factor I family, causes intellectual disability with macrocephaly.

Upcoming Events and Jobs

Seminar on Ethical, Legal and Social Implications of Genetics

Center for Research on Ethical/Legal/Social Implications of Psychiatric, Neurologic & Behavioral Genetics

Department of Psychiatry, Columbia University Medical Center

January 14th – Michelle Meyer, PhD, JD, Center for Translational Bioethics and Health Care Policy, Geisinger Health System

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Faculty at four University of California campuses are starting a new postdoctoral program focused on the epidemiology of Alzheimer's disease and other types of dementia. That means research into racial inequalities, vascular risks, and the social

factors that contribute to health. Postdocs will have one home campus — either Los Angeles, Davis, San Francisco, or Irvine — and collaborate with the other three campuses through a rotational program. Find out more here.

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