News, Literature, and Events in Braingenethics

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Braingenethics Update

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Major Psychiatric Disorders Share Brain Gene Activity

Shared Molecular Neuropathology Across Major Psychiatric Disorders Parallels Polygenic Overlap

Michael J. Gandal et al.

The predisposition to neuropsychiatric disease involves a complex, polygenic, and pleiotropic genetic architecture. However, little is known about how genetic variants impart brain dysfunction or pathology. This study used transcriptomic profiling as a quantitative readout of molecular brain-based phenotypes across five major psychiatric disorders—autism, schizophrenia, bipolar disorder, depression, and alcoholism, and identified patterns of shared and distinct gene-expression perturbations across these conditions. The degree of sharing of transcriptional dysregulation is related to polygenic (single-nucleotide polymorphism–based) overlap across disorders, suggesting a substantial causal genetic component. See further commentary in Science Magazine.

In the Literature

[Predictive Testing and Clinical Trials in Hungtington's Disease: An Ethical Analysis]

Cristina Sampaio et al.

Several potential Huntington's disease (HD) therapeutics are now reaching clinical development, raising ethical questions of whether clinical trials should include at risk individuals who choose not to undergo testing. This study examines 3 possible trial designs for interventions in premanifest HD using the 4 basic ethical principles.

[Effect of Low-Fat vs Low-Carbohydrate Diet on 12-Month Weight Loss in Overweight Adults and the Association with Genotype Pattern or Insulin Secretion: The DIETFITS Randomized Clinical Trial]

Christopher D. Gardner et al.

In this 12-month weight loss diet study, there was no significant difference in weight change between a healthy low-fat diet vs a healthy low-carbohydrate diet. Neither genotype pattern (low-fat or low-carbohydrate genotype) nor baseline insulin secretion was associated with the dietary effects on weight loss.

[Correction of Diverse Muscular Dystrophy Mutations in Human Engineered Heart Muscle by Single-Site Genome Editing]

Chengzu Long et al.

Duchenne muscular dystrophy (DMD) is associated with lethal degeneration of cardiac and skeletal muscle caused by more than 3000 different mutations in the X-linked dystrophin gene (*DMD*), most of which are are clustered in "hotspots." This proof-of-concept study suggests a way to use CRISPR/Cas9 genome editing to return a mutant engineered muscle to near-normal control levels by eliminating the underlying genetic basis of the

In the Media

[Two Psychologists Followed 1000 New Zealanders for Decades. Here's What They Found About How Childhood Shapes Later Life]

Douglas Starr

For nearly 30 years, Terrie Moffitt and Avshalom Caspi have been collaborating on one of the most comprehensive and probing investigations of human development ever conducted.

[Forget Me Not: Living With Early-Onset Alzheimer's]

Grace Niewijk

Jackie Frisk can no longer recall how many children she has, but she can still play the piano beautifully. This strange juxtaposition is one of many changes that have come with the progression of her Alzheimer's disease. Frisk is a participant in a trial at Jackson Laboratory, where researchers are interested in populations with varying expressions of Alzheimer's, including those with genetic predispositions for, but no disease phenotypes of, the disease.

[GWAS Uncovers Variants Linked to Symptoms, Progression of Alzheimer's, Parkinson's Disease]

GenomeWeb Staff Reporter

Two genome-wide association studies appearing in JAMA Neurology have begun to tease out how genetic risk variants contribute to neurodegenerative disease. In one, researchers found that a number of Alzheimer's disease-associated risk variants were associated with the accumulation of amyloid protein in the brain. Another found that Parkinson's disease risk variants are

disease.

ASO Therapy: Hope for Genetic Neurological Diseases
Christopher C. Muth
Newly approved treatments for spinal muscular atrophy and Duchenne muscular dystrophy, both neuromuscular diseases caused by rare genetic mutations, share a therapeutic approach: the use of antisense oligonucleotides (ASOs).

Analyzing the Genes Related to Nicotine Addiction or Schizophrenia via a Pathway and Network Based Approach
Ying Hu et al.
While there appears to be a close relationship between nicotine addiction and schizophrenia, the molecular mechanism underlying the high comorbidity of tobacco smoking and schizophrenia remains largely unclear. These results illustrate the complexity of this comorbidity.

Clustering of Neuropsychiatric Disease in First-Degree and Second-Degree Relatives of Patients With Amyotrophic Lateral Sclerosis
Margaret O'Brien et al.
There is increasing epidemiologic evidence of an association between Amyotrophic lateral sclerosis (ALS) and a wider spectrum of neurodegenerative and neuropsychiatric disorders among family members, including schizophrenia and psychotic illness and suicidal behavior. Using patients from the Irish ALS registry, finding that neuropsychiatric symptoms occur more frequently in kindreds than in controls.

MicroRNAs in CSF as Prodromal Biomarkers for Huntington Disease in the PREDICT-HD Study
Eric R. Reed et al.
cumulatively linked to motor and cognitive decline.

Toward an Optically Controlled Brain
Neus Feliu et al.
In the relatively new field of optogenetics, DNA is engineered into neurons to make them responsive to special light, allowing neurons to be modulated. A recent paper in Science successfully modulates neuronal activity in transgenic mice, even deep inside the brain. Such a method could lead the way for clinical applications to optically control neuronal dysfunctions, such as Parkinson's disease or even paralysis.
Read more in Stat and the original article in Science.

More In the Literature

Identification of Genetic Risk Factors in the Chinese Population Implicates a Role of Immune System in Alzheimer's Disease Pathogenesis
Xiaopu Zhou et al.
By performing a whole-genome sequencing study of Alzheimer's Disease (AD) in the Chinese population, the authors identified common variants of *GCH1* and *KCNJ15* that contribute to AD

Early microRNA biomarkers for Huntington disease (HD) might prove useful in identifying treatments that postpone disease onset. This study reports microRNAs in prodromal HD groups furthest from diagnosis where treatments are likely to be most consequential.

Damaging De Novo Mutations Diminish Motor Skills in Children on the Autism Spectrum

Andreas Buja et al.

In individuals with autism spectrum disorder (ASD), de novo mutations have previously been shown to be significantly correlated with lower IQ but not with the core characteristics of ASD. This study extends these findings by demonstrating that damaging de novo mutations in ASD individuals are also significantly correlated with measures of impaired motor skills, and proposes a new classification of phenotypic severity.

Functional Variants in the LRRK2 Gene Confer Shared Effects on Risk for Crohn's Disease and Parkinson's Disease

Ken Y. Hui

Crohn's disease and Parkinson's disease have separate disease mechanisms, but this study finds shared alleles in the LRRK2 gene that provide insight into their etiologies and may have major implications for both of their treatments.

risk. These variants may exert their functional effects through the immune system.

Transcriptomic Alterations During Ageing Reflect the Shift from Cancer to Degenerative Diseases in the Elderly

Peer Aramillo Irizar et al.

Disease epidemiology during ageing shows a transition from cancer to degenerative chronic disorders as dominant contributors to mortality in the old. This study confirms the existence of a similar shift at the genomic level, where a majority of shared risk alleles which increase the risk of cancer decrease the risk of chronic degenerative disorders and vice versa.

Aging and Neurodegeneration Are Associated with Increased Mutations in Single Human Neurons

Michael A. Lodato et al.

It has long been hypothesized that aging and neurodegeneration are associated with somatic mutation in neurons. This study found such mutations to increase approximately linearly with age, which may be important in understanding neurodegenerative, as well as other age-associated, disorders.

Genomic DNA Methylation Signatures Enable Concurrent Diagnosis and Clinical Genetic Variant Classification in Neurodevelopmental Syndromes

Erfan Aref-Eshghi et al.

Some pediatric developmental syndromes are the consequence of Mendelian inheritance of mutations in genes involved in DNA methylation, establishment of histone modifications, and chromatin remodeling. This study looked for syndrome-specific biomarkers to complement standard clinical diagnosis, finding as well that machine learning might

be useful in the diagnosis of ambiguous cases.

Upcoming Event

Looking for the Psychosocial Impacts of Genomic Information

Monday February 26th and Tuesday February 27th

The Faculty House, Columbia University

For the last quarter century, researchers have been asking whether genomic information might have negative psychosocial effects. Anxiety, depression, disrupted relationships, and heightened stigmatization have all been posited as possible outcomes—but not consistently found. At this conference, we will ask what accounts for the discrepancy between these hypothesized outcomes and the effects that have been documented in empirical studies. Are we asking the right questions? Using the right tools? Looking in the right places? Or was the expectation of large, negative psychosocial impacts of genomic information overblown to begin with? Either way, where does research into the ethical and psychosocial implications of genomic medicine go from here?

Hosted by the Center for Research on Ethical, Legal, and Social Implications of Psychiatric, Neurologic, and Behavioral Genetics, a collaborative project of Columbia University Medical Center and The Hastings Center.

More information **and live stream** here.

Upcoming Webinars

Two webinars sponsored by The Scientist will feature expert panels on neurodevelopment and neurodegenerative diseases.

Studying the Genetic Basis of Neurodevelopmental Channelopathies

Wednesday, March 7th, 2018, 2:30-4:00 pm

In this webinar, experts will discuss neurodevelopmental channelopathies, which

impact the responsiveness of cells in the central nervous system to typical electrochemical signals. These signal disruptions can range in severity, from mild to intense, leading to epilepsy and speech disturbances. The panelists will discuss their research in the genetics of channelopathies and their role in neurodevelopment.

Are All Neurodegenerative Diseases Made Equal?
Wednesday, April 11th, 2018, 2:30-4:00 pm
This webinar will focus on the neurodegenerative processes resulting in the development of diseases like Alzheimer's (AD), Parkinson's (PD), amyotrophic lateral sclerosis (ALS), and multiple sclerosis (MS). Recent studies have suggested common mechanisms underlying these pathologies. A panel of experts will share their research, discuss current therapeutic approaches, and offer their insights on the mechanisms that drive this array of neurodegenerative diseases.

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