News, Literature, and Events in Braingenethics

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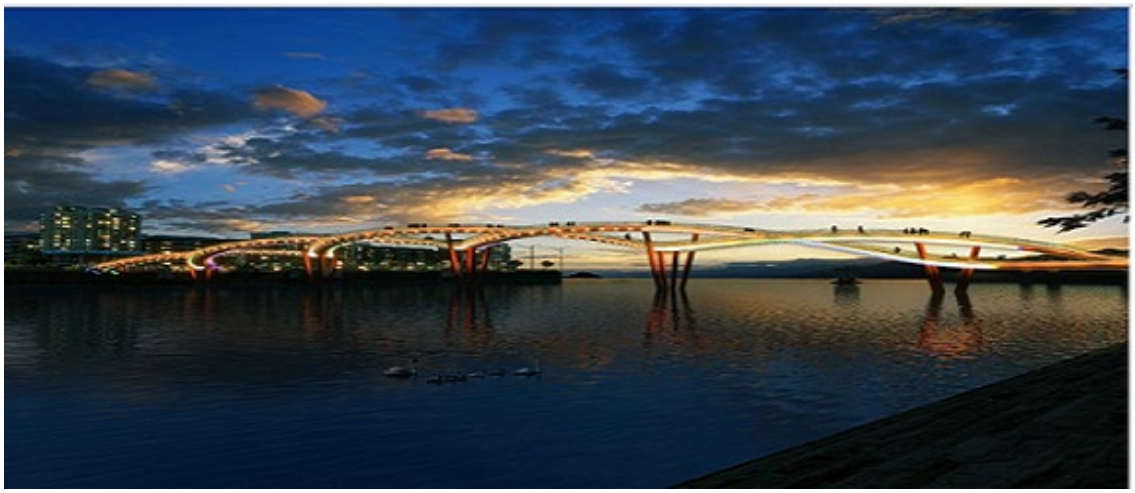

In the Media

In a First, Gene Therapy Halts a Fatal Brain Disease

Gina Kolata

A new study indicates that gene therapy can hold off adrenoleukodystrophy (ALD) without side effects, but only if it is begun when the only signs of deterioration are changes in brain scans.

Parents Lobby States to Expand Newborn Screening Test for Rare Brain Disorder

Anna Gorman

Only 5 states currently routinely test for it, but advocates argue that early testing for adrenoleukodystrophy (ALD) can dramaticallly improve outcomes for the generally fatal

In the Literature

Discord Over DNA: Ideological Responses to Scientific Communication about Genes and Race

Alexandre Morin-Chassé et al.

The American public's beliefs about the causes of social inequality vary greatly, with debates over the causes of racial inequality tending to be the most salient and divisive. This paper observes that when white citizens are exposed to media messages that emphasize the egalitarian implications of genetic similarity between racial groups, those on the left and right engage in biased assimilation, resulting in a “nature” (conservative) versus “nurture” (liberal) divide.

“Possibly Positive or Certainly Uncertain?": Participants’ Responses to

disorder.

[Four Brain Genes Help Explain Obsessive Compulsive Disorder]

Alice Klein

Four genes have been identified that are linked to obsessive compulsive disorder (OCD). They all play a role in the same brain circuit, and may help explain why people are more likely to have OCD if they have a relative with the condition.

[We Don't Want to Know What Will Kill Us]

Laura Spinney

Years of data on genetic testing reveal that when given the option, most people want less information, not more.

[Personal Genetic Testing Is Here. Do We Need It?]

Anahad O'Connor

Experts say many people are using a growing stream of genetic data to help them make better health decisions. But they also warn that some consumers may be led astray by genetic findings that are overblown or irrelevant.

[Severed Head of Eccentric Jeremy Bentham to Go on Display as Scientists Test DNA to See If He Was Autistic]

Sarah Knapton

In 2006, researchers Philip Lucas and Anne Sheeran suggested that Bentham's unique character was driven by Asperger's syndrome, after studying biographies which described a young Bentham as 'having few companions his own age'; and being 'morbidly sensitive.'

[Navajo Nation Reconsiders Ban on Genetic Research]

Sara Reardon

[Uncertain Diagnostic Results from Exome Sequencing]

Debra Skinner et al.

This study investigates clinicians' communications and patient/participant responses to uncertain diagnostic results arising from a clinical exome sequencing research study, contributing empirical data to the debate surrounding disclosure of uncertain genomic information. It finds that participants understood their uncertain results in ways that were congruent with clinical geneticists' communications.

[Misleading Guidance from Pharmacogenomic Testing]

Tahir Rahman

An analysis of the case of an involuntarily committed 25-year-old man with schizophrenia suggests that pharmacogenetic testing may provide some benefits, but cautions against overdetermining their utility, as the information they provide may be inadequate and in some cases harmful.

Genetics of Schizophrenia

[The Neurodevelopmental Origins of Schizophrenia in the Penumbra of Genomic Medicine]

Tribal leaders are developing a policy for genetic research and data sharing, potentially ending a 15-year moratorium.

In the Literature, cont.

Polygenic Hazard Scores in Preclinical Alzheimer Disease
Chin Hong Tan et al.
Identifying asymptomatic older individuals at elevated risk for developing Alzheimer disease (AD) is of clinical importance. Among 1,081 asymptomatic older adults, a recently validated polygenic hazard score (PHS) significantly predicted time to AD dementia and steeper longitudinal cognitive decline, even after controlling for APOE ε4 carrier status.

Loss of CLOCK Results in Dysfunction of Brain Circuits Underlying Focal Epilepsy
(more here**)**
Peijun Li et al.
Compared with controls, expression of Circadian Locomotor Output Cycles Kaput (CLOCK) is decreased in epileptogenic tissue. Data from mouse trials show that disruption of CLOCK alters cortical circuits and may lead to the generation of focal epilepsy.

The Genetics of Parkinson Disease
Lina Mastrangelo
Since 1997, the advances in the genetics of Parkinson Disease (PD) have expanded our understanding of this neurodegenerative disorder and they are opening up new ways to search for disease-modifying therapies. This chapter is a summary of the historical discoveries and latest progress in PD research.

Staging in Bipolar Disorder: From Theoretical Framework to Clinical Utility
Michael Berk et al.

Daniel R. Weinberger
This paper examines genomic and epigenetic evidence for neurodevelopmental origins of schizophrenia, and suggests that rather than defining the genetics, the primary public health challenge may be to define the functional state of the brain.

Genetic Insights into the Neurodevelopmental Origins of Schizophrenia
Rebecca Birnbaum & Daniel R. Weinberger
This review revisits the neurodevelopmental model of schizophrenia from a current genetics perspective, outlining the complex genetic basis of the disorder and highlighting gene expression and epigenetic analyses of post-mortem cortical tissue that suggest that early brain development mediates genetic risk associated with schizophrenia.

How Good Were Candidate Gene Guesses in Schizophrenia Genetics?
Patrick F. Sullivan
Researchers have been guessing at candidate genes for schizophrenia for over 40 years. The top 10 are familiar: BDNF, COMT, neuregulin 1, dysbindin, AKT1, DRD2, and DISC1. In this issue of Biological Psychiatry, Johnson et al. ask an important question: how good was our guesswork? They pose a contrast: do lists of the top 25 or the top 86 historical candidate genes for schizophrenia have, as a set, better evidence of association with schizophrenia? How good was the field at guessing?

Genome-Wide Association Analysis

The utility and validity of a staging model for bipolar disorder depend on its linkage to clinical outcome, treatment response and neurobiological measures. This paper aims to a) explore the current level of evidence supporting the descriptive staging of the syndromal pattern of bipolar disorder; b) describe preliminary attempts at validation; c) make recommendations for the direction of further studies; and d) provide a distillation of the potential clinical implications of staging in bipolar disorder within a broader transdiagnostic framework.

Genetic Heterogeneity in Depressive Symptoms Following the Death of a Spouse: Polygenic Score Analysis of the U.S. Health and Retirement Study

Benjamin W. Domingue et al.

A controversial hypothesis for the relationship between genes and depression is that genetic factors influence vulnerability to depression following stress. This paper's author tested whether genes buffer against depressogenic effects of life stress, and found that having a higher well-being polygenic score buffered against some increased depressive symptoms following a spouse's death.

Moderation of Genetic Influences on Alcohol Involvement by Rural Residency among Adolescents: Results from the 1962 National Merit Twin Study

Christal N. Davis et al.

Adolescents in rural and urban areas may experience different levels of environmental restrictions on alcohol use, with those in rural areas experiencing greater monitoring and less access to alcohol. Such restrictions may limit expression of genetic vulnerability for alcohol use, resulting in a gene–environment interaction. This study represents a partial replication in a novel

Identifies 30 New Susceptibility Loci for Schizophrenia

Zhiqiang Li et al.

An analysis of over 36,000 Chinese individuals identified seven Genome-Wide Significant (GWS) loci; three of these also were GWS in transancestry analyses, which identified 109 GWS loci, thus yielding a total of 113 GWS loci (30 novel) in at least one of these analyses. These results provide several lines of evidence supporting candidate genes at many susceptibility loci and highlight some pathways for further research.

Polygenic Risk Scores in Psychiatry

David Goldman

In this issue of Biological Psychiatry, Hartz et al. report evidence for common genetic origins of schizophrenia and addiction using a relatively new method, the polygenic risk score (PRS). Genome-wide association (GWA) has implicated many single nucleotide polymorphisms (SNPs) and genes in psychiatric disease, but identified few functional loci. Discovery of circuits, cells, and molecules integral to psychiatric diseases has been accomplished largely without the aid of GWA. However, there is reason for optimism for progress via integrative, big data analyses.

Schizophrenia and the Neurodevelopmental Continuum: Evidence from Genomics

Michael J. Owen et al.

The neurodevelopmental hypothesis for the pathogenesis of schizophrenia has become widely accepted. Despite this, the disorder is viewed as being nosologically distinct from syndromes such as

setting of the moderation of the genetic contribution to alcohol use by rural/urban residency, and suggests that SES differences may not explain this effect.

[Effects of Social Attitude Change on Smoking Heritability]

Laura Mezquita

Societal attitudes and norms to female smoking changed in Spain in the mid-twentieth century from a restrictive to a tolerant, and an even pro-smoking, posture, while social attitudes remained stable for males. The authors explored whether this difference in gender-related social norms influenced the heritability of two tobacco use measures, and found that that heritability is larger in a permissive social environment, whereas shared-environmental factors are more relevant in a society that is less tolerant to smoking.

autism spectrum disorders, attention-deficit/hyperactivity disorder (ADHD) and intellectual disability, which typically present in childhood and are grouped together as “neurodevelopmental disorders.” Findings reviewed in this paper support the view that schizophrenia is a disorder whose origins lie in disturbances of brain development, and that it shares genetic risk and pathogenic mechanisms with the early onset neurodevelopmental disorders.

Identification of Genetic Loci Jointly Influencing Schizophrenia Risk and the Cognitive Traits of Verbal-Numerical Reasoning, Reaction Time, and General Cognitive Function

Olav B. Smeland et al.

This analysis of genome-wide association studies found 21 genomic regions to be shared between schizophrenia and cognitive traits.These findings provide new insights into the common genetic basis underlying schizophrenia and cognitive function, suggesting novel molecular genetic mechanisms.

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