|MC:SUBJECT|

News, literature, and events in the ethical, social, and legal implications of psychiatric, neurologic, and behavioral genetics.

View this email in your browser

Braingenethics Update

No. 9 November 2014
braingenethics.cumc.columbia.edu/

In the Literature

Combined Influences of Genes, Prenatal Environment, Cortisol, and Parenting on the Development of Children's Internalizing Versus Externalizing Problems

By Kristine Marceau, Heidemarie K. Laurent, Jenae M. Neiderhiser, David Reiss, Daniel S. Shaw, Misaki N. Natsuaki, Phillip A. Fisher, Leslie D. Leve

Research suggests that genetic, prenatal, endocrine, and parenting influences across development individually contribute to internalizing and externalizing problems in children. The results of this study suggest that prenatal maternal drug use/symptoms and

Featured Collections

The Journal of Law, Medicine & Ethics: Special Issue: SYMPOSIUM: Clinical Integration of Next Generation Sequencing: A Policy Analysis

Clinical next generation sequencing (NGS) technologies are challenging existing regulatory paradigms. This collection advocates a coordinated policy approach, which first requires a comprehensive understanding of the existing regulatory and legal structures. In bringing these policy issues into conversation through this special issue for the Journal of Law,

children's morning cortisol levels are mechanisms of genetic and environmental influences on internalizing problems, but not externalizing problems, in childhood.

Genetic Influences on Brain Gene Expression in Rats Selected for Tameness and Aggression

By Henrike O. Heyne et al.

Interindividual differences in many behaviors are partly due to genetic differences, but the identification of the genes and variants that influence behavior remains challenging. Here, the authors studied an F2 intercross of two outbred lines of rats selected for tame and aggressive behavior toward humans for >64 generations. Through analyses of correlations between allele effects on behavior and gene expression, differential expression between the tame and aggressive rat selection lines, and correlations between gene expression and tameness in F2 animals, the researchers identify the genes Gltscr2, Lgi4, Zfp40, and Slc17a7 as candidate contributors to the strikingly different behavior of the tame and aggressive animals.

The Genetics of Impulsivity: Evidence for the Heritability of Delay Discounting

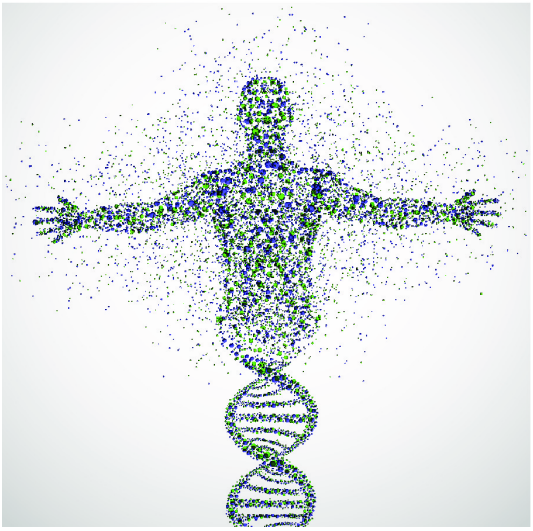
By Andrey P. Anokhin, Julia D. Grant, Richard C. Mulligan & Andre C. Heath

Delay discounting (DD), a decline in the subjective value of reward with increasing delay until its receipt, is an established behavioral model of impulsive choice. The goal of this study was to assess heritability of DD, an important aspect of its utility as an endophenotype. The authors provide the first evidence for heritability of both model-based and model-free DD measures and suggest that DD is a promising intermediate phenotype for genetic dissection of impulsivity and externalizing spectrum disorders.

Medicine & Ethics, the authors hope to lay the foundation for further discussion by a range of stakeholder groups with diverse and strong interests in the governance of NGS.

Nature Reviews Genetics: Web Collection: *Clinical Applications of Next-Generation Sequencing*

At this critical turning point, this collection highlights the breadth of applications of next-generation sequencing technologies in the clinic and the importance of the insights that are being gained through these methods to improve health.



In the News

Whole-Genome Sequencing of the World's Oldest People

By Hinco J. Gierman et al.

Supercentenarians (110 years or older) are the world's oldest people. Seventy four are alive worldwide, with twenty two in the United States.

[The Molecular Bases of the Suicidal Brain]
By Gustavo Turecki

Suicide ranks among the leading causes of death around the world and takes a heavy emotional and public health toll on most societies. Both distal and proximal factors contribute to suicidal behaviour. Distal factors — such as familial and genetic predisposition, as well as early-life adversity — increase the lifetime risk of suicide. They alter responses to stress and other processes through epigenetic modification of genes and associated changes in gene expression, and through the regulation of emotional and behavioural traits. Proximal factors are associated with the precipitation of a suicidal event and include alterations in key neurotransmitter systems, inflammatory changes and glial dysfunction in the brain. This Review explores the key molecular changes that are associated with suicidality and discusses some promising avenues for future research.

Incidental Findings

[Reporting Genomic Secondary Findings: ACMG Members Weigh In]
By Maren T. Scheuner et al.

The aim of this study was to survey American College of Medical Genetics and Genomics members about secondary findings from clinical genome-scale sequencing. The authors concluded that the American College of Medical Genetics and Genomics should update a list of genes to be assessed when clinical genome-scale sequencing is performed. Informed consent is necessary, and reporting of secondary findings should be optional. Research on implementation of

The authors performed whole-genome sequencing on 17 supercentenarians to explore the genetic basis underlying extreme human longevity. The entire list of rare protein-altering variants and DNA sequence of all 17 supercentenarian genomes is available as a resource to assist the discovery of the genetic basis of extreme longevity in future studies.

[A Mother's Soothing Presence Makes Pain Go Away – and Changes Gene Activity in the Infant Brain]
By Regina Sullivan

A mother's 'TLC' not only can help soothe pain in infants, but it may also impact early brain development by altering gene activity in a part of the brain involved in emotions, according to this new study.

In the Literature

[Familial Recurrence of Autism Spectrum Disorder: Evaluating Genetic and Environmental Contributions]
By Neil Risch, Thomas J. Hoffmann, Meredith Anderson, Lisa A. Croen, Judith K. Grether & Gayle C. Windham

This study was designed to examine the pattern of familial recurrence of autism spectrum disorder (ASD) in terms of genetic and environmental contributions related to timing of birth. The results support genetic susceptibility in the familial recurrence of ASD along with factors related to timing of birth.

[Genetic Epidemiology and Insights into Interactive Genetic and Environmental Effects in Autism Spectrum Disorders]
By Young Shin Kim & Bennett L. Leventhal

Understanding the pathogenesis of Neurodevelopmental Disorders (NDDs) has

secondary findings reporting is needed.

[ACMG Recommendations for Reporting of Incidental Findings in Clinical Exome and Genome Sequencing]

By Robert C. Green et al.

In clinical exome and genome sequencing, there is a potential for the recognition and reporting of incidental or secondary findings unrelated to the indication for ordering the sequencing but of medical value for patient care. The American College of Medical Genetics and Genomics (ACMG) recently published a policy statement on clinical sequencing that emphasized the importance of alerting the patient to the possibility of such results in pretest patient discussions, clinical testing, and reporting of results. The ACMG recommends that laboratories performing clinical sequencing seek and report mutations of the specified classes or types in the genes listed here. This evaluation and reporting should be performed for all clinical germline (constitutional) exome and genome sequencing, including the "normal" of tumor-normal subtractive analyses in all subjects, irrespective of age but excluding fetal samples.

[The Cost-effectiveness of Returning Incidental Findings from Next-generation Genomic Sequencing]

By Caroline S. Bennette, Carlos J. Gallego, Wylie Burke, Gail P. Jarvik & David L. Veenstra

The American College of Medical Genetics and Genomics (ACMG) recommended that clinical laboratories performing next-generation sequencing analyze and return

proven to be challenging. Using Autism Spectrum Disorder (ASD) as a paradigmatic NDD, this paper reviews the existing literature on the etiologic substrates of ASD and explores how genetic epidemiology approaches including gene-environment interactions (GxE) can play roles in identifying factors associated with ASD etiology.

Commentaries

[NIPS: Microdeletions, Macro Questions]

By Katie Stoll

This blog critique questions the expansion of noninvasive prenatal screening in the absence of validation studies.

CEER Seminar

Prenatal Diagnosis: How Much Should We Know?

Emerging genomic technology allows us to provide increasing information about the developing fetus. This raises a number of questions about how much we should know about these findings that will be discussed in this presentation.

Ronald J. Wapner, MD
Director of Reproductive Genetics
Vice Chair of Research
Department of Obstetrics & Gynecology
Columbia University Medical Center

Wednesday, December 3, 2014
4:00-5:00pm
Rm 405A and B, Educational Center, Irving Institute for Clinical and Translational Research

pathogenic variants for 56 specific genes it considered medically actionable. The authors aimed to evaluate the clinical and economic impact of returning these results. Returning incidental findings is likely cost-effective for certain patient populations. Screening of generally healthy individuals is likely not cost-effective based on current data, unless next-generation sequencing costs less than$500.

10th Floor, Presbyterian Hospital (PH) Building

622 W. 168th Street

To contribute a news item, an academic article, or an event on the ethical, legal, and social implications of psychiatric, neurological, and behavioral genetics research please email us.

Click here to subscribe to the Braingenethics Update!

Columbia University Medical Center | The Hastings Center

Email us at:
info@brangenethics.cumc.columbia.edu

Please visit our website for more information:
braingenethics.cumc.columbia.edu