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

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In the Literature

Return of Individual Genetic Results in a High-Risk Sample: Enthusiasm and Positive Behavioral Change

Sarah M. Hartz et al.

The goal of this study was to examine participant responses to disclosure of genetic results in a minority population at high risk for depression and anxiety. Eighty-two subjects in a genetic study of nicotine dependence were offered personalized genetic results to evaluate genetic risks for five complex diseases. Participants returned 4–8 weeks after enrollment for in-person genetic counseling interviews and evaluation of baseline measures followed by a telephone call to assess responses to

Meta-analysis of the Heritability of Human Traits Based on Fifty Years of Twin Studies

By Tinca J.C. Polderman et al.

The authors report a meta-analysis of twin correlations and reported variance components for 17,804 traits from 2,748 publications including 14,558,903 partly dependent twin pairs, virtually all published twin studies of complex traits. Estimates of heritability cluster strongly within functional domains, and across all traits the reported heritability is 49%. For a majority (69%) of traits, the observed twin

results. Even in an underserved population at high risk for adverse psychological reactions, subjects responded positively to personalized genetic results.

Can Targeted Genetic Testing Offer Useful Health Information to Adoptees?

By Thomas May, Kimberly A. Strong, Muin J. Khoury, James P. Evans

In 2004, the US Surgeon General launched the Family History Public Health Initiative to increase awareness and discussions regarding family health history (FHx). FHx reflects the combined influences of shared genetic, behavioral, and environmental factors in families, yet many segments of the population lack adequate access to the genetic component. This article focuses on the needs of adoptees, whose lack of genetic FHx normally reflects separation from biological parents.

Genetics in Child and Adolescent Psychiatry: Methodological Advances and Conceptual Issues

By: Sarah Hohmann, Nicoletta Adamo, Benjamin B. Lahey, Stephen V. Faraone, & Tobias Banaschewski

Discovering the genetic basis of early-onset psychiatric disorders has been the aim of intensive research during the last decade. This article selectively summarizes results of genetic research in child and adolescent psychiatry by using examples from different disorders and discussing methodological issues, emerging questions, and future directions. Additionally, it focuses on how to link genetic causes of disorders with physiological pathways and highlights some ethical aspects

correlations are consistent with a simple and parsimonious model where twin resemblance is solely due to additive genetic variation. They provide the most comprehensive analysis of the causes of individual differences in human traits thus far and will guide future gene-mapping efforts.

In the News

Infidelity Lurks in Your Genes

Recent research has found that women with certain variants of the vasopressin receptor gene are much more likely to engage in “extra pair bonding,” the scientific euphemism for sexual infidelity. Additionally, there is a significant association between one variant of the oxytocin receptor gene and marital discord and lack of affection for one’s partner. While genetic variants are not the whole picture, Richard Friedman writes that there are compelling reasons to see infidelity as influenced by our genes.

"Infidelity Gene" Hyped in the News

This response, by John Horgan, critiques the piece above for scientific inaccuracies and exaggerations in regard to the genetic connection to infidelity. It specifically assesses the citations and sources with the introduction of contradictory evidence.

Neurons Rewrite Their DNA On

connected to genetic research in child and adolescent psychiatry.

Brains, Genes, and Primates
By Juan C. I. Belmonte et al.
While the mouse model has been useful in developing a wide array of genetic tools, it has some significant limitations. This article argues that understanding the primate brain may bridge the gap between what can be learned from the mouse regarding human anatomy, physiology, cognition, and behavior. It discusses the bioethical considerations of using primate brains to study human brains and disorders with a look to future advances.

Meta-analysis of Genome-wide Association Studies for Neuroticism, and the Polygenic Association with Major Depressive Disorder
By: Genetics of Personality Consortium
The authors identify a novel locus—the MAGI1 locus—for neuroticism. The variant is located in a known gene that has been associated with bipolar disorder and schizophrenia in previous studies. In addition, the study shows that neuroticism is influenced by many genetic variants of small effect that are either common or tagged by common variants. These genetic variants also influence Major Depressive Disorder.

Evaluating Historical Candidate Genes for Schizophrenia
By Martilias S. Farrell et al.
This review considers the current status of 25 historical candidate genes for schizophrenia (for example, COMT, DISC1, DTNBP1 and NRG1). This

The Go
Scientists have discovered that neurons use minor "DNA surgeries," through the process of DNA methylation, to toggle their activity levels all day, every day. This methylation changes expression in Tet3 as a mechanism used by neurons to maintain relatively consistent levels of synaptic activity so that neurons can remain responsive to the signaling around them. Since these activity levels are important in learning, memory and brain disorders, it could shed light on a range of important questions.

The Wanderlust Gene: Why Some People Are Born To Travel
As outlined in this blog post, the DRD4-7r gene variant is associated with a history of travel and has been dubbed the "wanderlust gene." This variant is connected to curiosity, exploration, and its properties may go as far back as initial migration patterns in human history.

Is There Really a 'Wanderlust Gene'?
The Elite Daily article listed above provides an oversimplification of how DRD4-7r operates. The gene, which affects dopamine receptors, was actually selected for as people migrated and did not cause them to migrate. While the gene is associated with characteristics that many would consider similar to a person with

evaluation includes a meta-analysis of the candidate gene literature, incorporation of the results of the largest genomic study yet published for schizophrenia, ratings from informed researchers who have published on these genes, and ratings from 24 schizophrenia geneticists. On the basis of current empirical evidence and mostly consensual assessments of informed opinion, it appears that the historical candidate gene literature did not yield clear insights into the genetic basis of schizophrenia.

Optogenetics and the Circuit Dynamics of Psychiatric Disease
By Karl Deisseroth, Amit Etkin, & Robert C. Malenka
Optogenetics is a method for delivering millisecond-precision control (for activation or inhibition) to targeted cells using light within mammals. The components of this method, as practiced today, involve (1) lasers and fiber optics for light delivery into the nervous system and (2) genes called microbial opsins, which encode light-activated proteins that regulate ion conductance across membranes. Constituted by single genes, these microbial opsins can be targeted using a toolbox of genetic techniques, thereby specifying light-induced current flow in cells defined by function and anatomy.

Excess of Runs of Homozygosity Is Associated with Severe Cognitive Impairment in Intellectual Disability
By: Ilaria Gandin et al.
While the harmful effects of inbreeding are well known by geneticists, the effects of inbreeding on the degree of wanderlust, the connection is not strong enough to imply such causation.

Genetics of Depression: Could a Test Have Prevented the Germanwings Catastrophe?
In light of pilot Andrew Lubitz's suicide by intentionally crashing the Germanwings flight, some have asked if a genetic test for depression might have been useful. Since depression is a complex condition, it is unlikely that a genetic test would provide a key in such a case. Gene environment interactions and the difficulty of diagnosing the condition lead the author to be skeptical that a genetic test is the answer.

Commentaries

Guest Post: PPV Puffery? Sizing Up NIPT Statistics
By Katie Stoll and Heidi Lindh
The importance of the Positive Predictive value (PPV) in interpreting Noninvasive Prenatal Testing (NIPT) results is increasingly on the minds of

intellectual disability produced are still poorly investigated. These researchers conducted a detailed analysis of the homozygosity regions in a cohort of 612 patients with intellectual disabilities of different degrees. In accord with the recent findings regarding autism and other neurological disorders, this study reveals the important role of autosomal recessive variants in intellectual disability. The amount of homozygosity seems to modulate the degree of cognitive impairment regardless of the intellectual disability's cause.

Altered MTORC1 Signaling in Multipotent Stem Cells from Nearly 25% of Patients with Nonsyndromic Autism Spectrum Disorders

By: Angela M. Suzuki et al.

Functional studies addressing mTORC1-signaling activity in accessible sources of cells from patients with nonsyndromic Autism Spectrum Disorder (ASD) are lacking. In this study, the authors have made use of the cultured stem cells from human exfoliated deciduous teeth derived from nonsyndromic ASD patients, a model system that, albeit non-neural, the authors have recently shown to be suitable to explore dysregulated pathways and biological processes in ASD to investigate this important and yet poorly explored question.

Dysregulation of MiR-34a Links Neuronal Development to Genetic Risk Factors for Bipolar Disorder

By Sabine Bavamian et al.

Given their prominent role in brain function and disease, the authors hypothesized that microRNAs might be

providers as evidenced by frequent discussions, presentations, and publications on the topic. The growing number of laboratories that offer some version of NIPT presents a significant challenge for healthcare providers who are struggling to navigate the various testing options to determine what is in the best interest of their patients. Honest communication about test performance metrics must be available to providers so that they can provide accurate counseling to patients making critical decisions about their pregnancies.

Genetically Modified Humans? Seven Reasons to Say "No"

By the Center for Genetics and Society

Researchers at Sun Yat-sen University in Guangzhou, China published a paper on April 18, 2015, detailing the first use of the "gene editing" technology CRISPR in human embryos. Gene therapy, an application of this technology to reproductive cells presents seven core ethical issues to consider.

Splice of Life

By Nature Editorial Staff

In light of recent advances in germline editing, now is a good time for a public debate about gene editing in sperm, eggs, and embryos. The latest research examines the ethical dimensions and possibilities, but these advances must be understood in context. Preimplantation genetic diagnosis and selection of healthy embryos during *in vitro* fertilization already provides a safer alternative for avoiding genetic disease in newborns — as can prenatal screening and

of importance for bipolar disorder (BD). They have shown that levels of miR-34a, which is predicted to target multiple genes implicated as genetic risk factors for BD, are increased in postmortem cerebellar tissue from BD patients, as well as in BD patient-derived neuronal cultures generated by reprogramming of human fibroblasts into induced neurons or into induced pluripotent stem cells subsequently differentiated into neurons. They propose that miR-34a serves as a critical link between multiple etiological factors for BD and its pathogenesis through the regulation of a molecular network essential for neuronal development and synaptogenesis.

Brain-specific Foxp1 Deletion Impairs Neuronal Development and Causes Autistic-like Behavior
By Claire Bacon et al.
Mutations in the Forkhead box FOXP1 gene have been linked to intellectual disability, autism spectrum disorder and language impairment, suggesting that this mutation may play a central role in various cognitive and social processes. To understand the role of Foxp1 in the context of neurodevelopment leading to alterations in cognition and behavior, the authors generated mice with a brain-specific Foxp1 deletion. The mutant mice were viable and allowed for the first time the analysis of pre- and postnatal neurodevelopmental phenotypes, which included a pronounced disruption of the developing striatum and more subtle alterations in the hippocampus.

Transcriptome Sequencing and Genome-wide Association Analyses

abortion. The diseases for which gene editing would be superior are few.

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.

Events

Center Seminar: Why I Am Skeptical about the Molecular Genetics of Very Complex Human Behavior
Eric Turkheimer, PhD
Department of Psychology, University of Virginia

Although it is very well established that no aspect of human behavior is completely independent of genetic background, understanding the specific genetic etiology of behavior has proven far more difficult than had been anticipated. A widely held view is that despite current frustrations, progress on the genetics of complex behavior is just a matter of time, technology and, especially, sample size. Turkheimer suggest that the problems run deeper, and will resist straightforward technological solutions

Wednesday, June 10, 2015 3:00-4:00pm (note new earlier time)
Rm 405A and B, Educational Center, Irving Institute for Clinical and Translational Research
10th Floor, Presbyterian Hospital (PH) Building
622 W. 168th Street

Reveal Lysosomal Function and Actin Cytoskeleton Remodeling in Schizophrenia and Bipolar Disorder

By Zhongming Zhao et al.

The authors conducted whole transcriptome analysis of post-mortem brain tissues (cingulate cortex) from schizophrenia, bipolar disorder and control subjects, and identified differentially expressed genes in these disorders. They found 105 and 153 genes differentially expressed in Schizophrenia (SCZ) and Bipolar Disorder (BPD), respectively. By comparing the t-test scores, they found that many of the genes differentially expressed in SCZ and BPD are concordant in their expression level. Using genome-wide association data from the Psychiatric Genomics Consortium, they found that these differentially and concordantly expressed genes were enriched in association signals for both SCZ ($P<10-7$) and BPD ($P=0.029$). This is the first time that a substantially large number of genes show concordant expression and association for both SCZ and BPD.

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Human Genome Project: History and Assessment

By Hub Zwart

International Encyclopedia of Social & Behavioral Sciences 2nd ed. Oxford Elsevier, 311-317.

By setting up a flanking program devoted to anticipating and addressing the ethical, legal, and social implications of genomics, the Human Genome Project (HGP) has had a substantial influence on the social sciences and humanities fields involved in studying contemporary science. In this article, the HGP is placed in a historical perspective as a key chapter in the history of the life sciences. The author assesses what the impact of the HGP has been, both for the life sciences as such and for the society in a broader sense, arguing that despite falling short of its stellar, revolutionary expectations its cultural relevance has been quite significant.

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