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

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The next Braingenethics Update (Vol. 2, No. 7) will appear in September 2015.

In the Literature

[Ethical Issues Associated with Genetic Counseling in the Context of Adolescent Psychiatry]

By Jane Ryan, Alice Virani, and Jehannine C. Austin

Psychiatric genetic counseling is emerging as an important service that fills a growing need to reframe understandings of the causes of mental health disorders. The authors define

[The Mixed-Up Brothers of Bogotá]

By Susan Dominus

After a hospital error, two pairs of Colombian identical twins were raised as two pairs of fraternal twins. This is the story of how they found one another — and of what happened next.

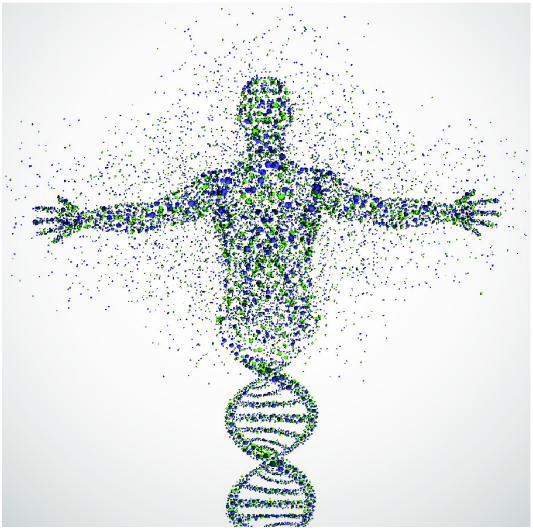
psychiatric genetic counseling and address important ethical concerns (they particularly give attention to the principles of autonomy, beneficence, non-maleficence and justice) that must be considered in the context of its application in adolescent psychiatry, whilst integrating evidence regarding patient outcomes from the literature.

[Points to Consider: Ethical, Legal, and Psychosocial Implications of Genetic Testing in Children and Adolescents]
By Jeffrey R. Botkin et al.

This statement represents current opinion by the American Society of Human Genetics (ASHG) on the ethical, legal, and social issues concerning genetic testing in children. After a brief review of the 1995 joint statement from ASHG and the American College of Medical Genetics and Genomics (ACMG), the authors describe major changes in genetic technologies in recent years. This statement offers points to consider on a broad range of test technologies and their applications in clinical medicine and research. It also makes recommendations regarding record and communication issues.

[Genomic Futures of Prenatal Screening: Ethical Reflection]
By Wybo Dondorp et al.

The practice of prenatal screening is undergoing important changes as a result of the introduction of genomic testing technologies at different stages of the



In the News

[First Robust Genetic Links to Depression Emerge]
By Heidi Ledford

In Nature this week, one study reports the first two genetic markers reproducibly linked to major depressive disorder, one of the leading causes of disability globally. The findings could guide biologists to new drugs, and could one day be used to aid diagnosis. But many in the field are excited that the markers have been unearthed at all. The results look set to end years of debate over whether sequences for such a complex disorder could be found — and this study may serve as a framework for future attempts to collect data from tens of thousands of people.

[About Human Germline Gene Editing]
By Center for Genetics and Society

screening trajectory. It is expected that eventually it will become possible to routinely obtain a comprehensive 'genome scan' of all fetuses. Although this will still take several years, there are clear continuities between present developments and this future scenario. As this review shows, behind the still limited scope of screening for common aneuploidies, a rapid widening of the range of conditions tested for is already taking shape at the post-invasive testing stage. But the continuities are not just technical; they are also ethical.

Comparison of Informed Consent Preferences for Multiplex Genetic Carrier Screening among a Diverse Population

By Ashley Reeves and Angela Trepanier

Multiplex genetic carrier screening is increasingly being integrated into reproductive care. Obtaining informed consent becomes more challenging as the number of screened conditions increases. Implementing a model of generic informed consent may facilitate informed decision-making. Participants were asked to determine which of two generic informed consent scenarios they preferred: a brief versus a detailed consent. A generic consent was perceived to provide sufficient information for informed decision making regarding multiplex carrier screening with most preferring the detailed to the brief. Individual attitudes rather than demographic variables influenced preferences regarding how much information should be included in the generic consent.

In April 2015, a research team at Sun Yat-sen University in China published a report of an experiment in which they used CRISPR to edit a gene associated with the blood disease beta-thalassemia in non-viable human embryos. The experiments were largely unsuccessful. But as gene editing tools are refined in labs around the world, they are expected to allow easier, cheaper, and more accurate insertion or deletion of genes than ever before. This controversy marks a new chapter in the debate about "genetically engineering" humans.

Sparse Whole-Genome Sequencing Identifies Two Loci for Major Depressive Disorder

By CONVERGE Consortium

Major depressive disorder (MDD) poses a major challenge to genetic analysis. To date, no robustly replicated genetic loci have been identified, despite analysis of more than 9,000 cases. Here, using low-coverage whole-genome sequencing of 5,303 Chinese women with recurrent MDD selected to reduce phenotypic heterogeneity, and 5,337 controls screened to exclude MDD, the authors identified, and subsequently replicated in an independent sample, two loci contributing to risk of MDD on chromosome 10: one near the SIRT1 gene ($P = 2.53 \times 10-10$), the other in an intron of the LHPP gene ($P = 6.45 \times 10-12$). Analysis of 4,509 cases with a severe subtype of MDD, melancholia, yielded an increased genetic signal at the SIRT1 locus. They attribute their success to the recruitment of relatively homogeneous cases with severe illness.

[Health-care Professionals' Responsibility to Patients' Relatives in Genetic Medicine: A Systematic Review and Synthesis of Empirical Research]
By Sandi Dheensa, Angela Fenwick, Shiri Shkedi-Rafid, Gillian Crawford & Anneke Lucassen

The authors argue that health-care professionals can sometimes share genetic information without breaching confidentiality and that they could factor into their considerations the potential harm to family dynamics of nondisclosure.

[Seven Questions for Personalized Medicine]
By Michael J. Joyner and Nigel Paneth

Personalized or precision medicine maintains that medical care and public health will be radically transformed by prevention and treatment programs more closely targeted to the individual patient. These interventions will be developed by sequencing more genomes, creating bigger biobanks, and linking biological information to health data in electronic medical records (EMRs) or obtained by monitoring technologies. Yet the assumptions underpinning personalized medicine have largely escaped questioning. The authors seek to stimulate a more balanced debate by posing seven questions for the advocates of personalized medicine.

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[Epigenetic Dysregulation in the Prefrontal Cortex of Suicide Completers]
By Eberhard Schneider et al.

The suicide liability of an individual appears to be influenced by many genetic factors of small effect size as well as by environmental stressors. To identify epigenetic marks associated with suicide, which is considered the endpoint of complex gene-environment interactions, the authors compared the cortex DNA methylation patterns of 6 suicide completers versus 6 non-psychiatric sudden-death controls, using Illumina 450K methylation arrays. Consistent with a multifactorial disease model, we found DNA methylation changes in a large number of genes, but no changes with large effects reaching genome-wide significance. Global methylation of all analyzed CpG sites was significantly (0.25 percentage point) lower in suicide than in control brains, whereas the vast majority (97%) of the top 1,000 differentially methylated regions (DMRs) were higher methylated (0.6 percentage point) in suicide brains.

[Serotonin Transporter Polymorphisms (5-HTTLPR) in Emotion Processing: Implications from Current Neurobiology]
By Rune Jonassen and Nils Inge Landrø

The serotonin transporter gene SLC6A4 has been studied more than any other single candidate gene in the field of neurobiology. Transcription of the serotonin transporter gene is modulated by a polymorphic region, 5-HTTLPR, near the promoter. 5-HTTLPR genotype has

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been associated with individual variation in emotion processing, brain structure, and brain function. The authors present an updated review of the biological literature on the serotonin transporter polymorphism and examine the clinical implications of discoveries about the role of serotonin and 5-HTTLPR genotype in neural plasticity and behavioral malleability.

The BDNF Valine 68 to Methionine Polymorphism Increases Compulsive Alcohol Drinking in Mice that Is Reversed by Tropomyosin Receptor Kinase B Activation
By Vincent Warnault et al.

The valine 66 to methionine (Met) polymorphism within the brain-derived neurotrophic factor (BDNF) sequence reduces activity-dependent BDNF release and is associated with psychiatric disorders in humans. Alcoholism is one of the most prevalent psychiatric diseases. Here, the authors tested the hypothesis that this polymorphism increases the severity of alcohol abuse disorders. Their findings suggest that carrying this BDNF allele increases the risk of developing uncontrolled and excessive alcohol drinking that can be reversed by directly activating the BDNF receptor, tropomyosin receptor kinase B. Importantly, this work identifies a potential therapeutic strategy for the treatment of compulsive alcohol drinking in humans carrying the Met66BDNF allele.

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