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Foreword for inaugural issue of Journal of Neurodevelopmental Disorders

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In 1986, William Greenough and Janice Juraska edited a volume entitled *Developmental Neuropsychobiology*. This poly-syllabic title reflected a multi-disciplinary ambition. As they noted in the introduction, "A motivating force behind the organization of this book was our perception of the mutual isolation of the fields of developmental neuroscience and developmental psychobiology. Each has its separate societies, journals, and international meetings, and there is remarkably little overlap in membership and even less in attendance at meetings" [9]. This was probably not the first, and certainly not the last, well-intentioned assault on the barriers between various neurodevelopmental disciplines. Yet 23 years later we still lack a unified, integrated science of the development of brain and behavior. We have increasingly robust fields of developmental neuroscience, developmental psychobiology, developmental psychology and developmental psychopathology, but these remain silos with their own professional societies, training programs, and journals. This cultural balkanization is even manifested in the languages used to describe developmental processes: "epigenetics," "imprinting," and "stress" have different meanings in these closely related disciplines. Beyond the cultural separation, the lack of a unified science prevents insights in one field from informing others, leaving all of us with less understanding of development than might be possible by combining diverse approaches.

The balkanization of disciplines is matched by a tendency to study neurodevelopmental disorders in silos. With Mendelian disorders, there is an argument for recognizing the unique features of Fragile X or Turner's Syndrome. But much has been lost by not studying how these syndromes overlap with a range of developmental disorders. We now understand that defined genomic lesions can result in heterogeneous phenotypes, but we need new insights into the mechanisms by which the same apparent lesion, such as the chromosome 1q21.1 deletion, leads to autism, mental retardation, or microcephaly [12]. For non-Mendelian disorders, such as autism, dyslexia, and neurotoxicologic developmental syndromes, the silo approach of research often fails to capture the reality of the clinic, where children are more likely to have many "disorders" rather than fit neatly into any single category of the current diagnostic manual.

For many reasons the time has come to bring these disparate fields together. As Freeman Dyson said of astronomy, new tools are more likely to bring change than new concepts [7]. Embryonic stem cells and induced pluripotent stem cells can now be differentiated into specific families of neurons [5]. These cells will open up reverse translational science: moving from the clinic back to the lab to explore how genetic variation leads to altered neural development. Whole genome epigenomics promises to map the fingerprints of experience during development, allowing a molecular understanding of how early experience can have enduring effects on behavior [1]. And with cellular imaging we can watch axons and dendrites find each other and follow changes in synaptic density in real time in the whole organism [10]. Each of these tools—and there are many others—permits a new approach to old problems by crossing the barriers from molecular or cellular biology to behavior.

Beyond new tools, there is unprecedented excitement in the study of neurodevelopmental disorders, especially Mendelian disorders such as Fragile X syndrome, Rett syndrome, and tuberous sclerosis [2, 3, 8]. For many Mendelian neurodevelopmental disorders, transgenic animals manifest key features of the clinical syndrome. These

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experimental model animals allow rigorous investigation of how these disorders develop, identifying the earliest phases of pathophysiology and, in some cases, revealing new targets for treatment [4, 6, 13]. While this approach has not yet proven itself for complex disorders, such as autism, there is every reason to believe that rare, highly penetrant mutations will be identified which can be studied in the same way as causal mutations for Mendelian disorders.

The most compelling reason for an integrative approach to neurobehavioral development is the public health mandate. Mental disorders are increasingly recognized as *the* chronic disorders of young people. These illnesses are common, usually begin before age 25 [11], and are disabling for many Americans. We recognize that many of these disorders, from autism to attention deficit hyperactivity disorder to schizophrenia, can be addressed as brain disorders. We understand each of these illnesses as developmental disorders, or more specifically as developmental brain disorders, resulting from early alterations in brain development, whether the symptoms become manifest before age 3 (autism), during early childhood (ADHD), before adolescence (anxiety disorders) or during (or after) adolescence (schizophrenia, mood disorders, and addictive disorders). The important insight to inform a neurodevelopmental approach is that the behavioral signs and symptoms are likely a late stage of the disorder. To reduce the disability of these mental disorders, we will need to detect them early and intervene before the behavioral symptoms become manifest. This preemptive strategy has transformed our approach to heart disease and cancer. For preemptive medicine to transform our approach to mental disorders, we will need a better understanding of the trajectory of these illnesses as developmental brain disorders.

The need for a better understanding of normal and atypical development in mental disorders brings us to the great promise and the great challenge of this new journal, Journal of *Neurodevelopmental Disorders.* With 5246 journals currently indexed in PubMed [14], one might ask whether we need yet another journal. In this case, the answer is a resounding "Yes," especially if this new journal can address the need for an integrative approach to both normal and abnormal development. The challenge will be to foster developmental science that crosses traditional barriers between psychology and biology, between human and non-human research, and between mechanistic and descriptive studies. There has never been a better time for this integration and never a greater need.

References

1. Barski A, Cuddapah S, Cui K, Roh TY, Schones DE, Wang Z, Wei G, Chepelev I, Zhao K. High-resolution profiling of histone methylations in the human genome. Cell 2007;129:823–37.
2. Bear MF, Huber KM, Warren ST. The mGluR theory of fragile X mental retardation. Trends Neurosci 2004;27:370–7.
3. Chahrour M, Zoghbi HY. The story of Rett syndrome: from clinic to neurobiology. Neuron 2007;56:422–37.
4. de Vrij FM, Levenga J, van der Linde HC, Koekkoek SK, De Zeeuw CI, Nelson DL, Oostra BA, Willemsen R. Rescue of behavioral phenotype and neuronal protrusion morphology in Fmr1 KO mice. Neurobiol Dis 2008;31:127–32.
5. Dimos JT, Rodolfa KT, Niakan KK, Weisenthal LM, Mitsumoto H, Chung W, Croft GF, Saphier G, Leibel R, Goland R, Wichterle H, Henderson CE, Eggan K. Induced pluripotent stem cells generated from patients with ALS can be differentiated into motor neurons. Science 2008;21:1218–21.
6. Dolen G, Osterweil E, Rao BS, Smith GB, Auerbach BD, Chattarji S, Bear MF. Correction of fragile X syndrome in mice. Neuron 2007;56:955–62.
7. Dyson FJ. Imagined worlds. Cambridge, Mass.: Harvard University Press; 1997.
8. Ehninger D, Han S, Shilyansky C, Zhou Y, Li W, Kwiatkowski DJ, Ramesh V, Silva AJ. Reversal of learning deficits in a Tsc2 +/− mouse model of tuberous sclerosis. Nat Med 2008;14:843–8.
9. Greenough WT, Juraska JM. Developmental neuropsychobiology. Orlando: Academic; 1986.
10. Javaherian A, Cline HT. Coordinated motor neuron axon growth and neuromuscular synaptogenesis are promoted by CPG15 in vivo. Neuron 2005;45:505–12.
11. Kessler RC, Berglund P, Demler O, Jin R, Merikangas KR, Walters EE. Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the National Comorbidity Survey Replication. Arch Gen Psychiatry 2005;62:593–602.
12. Mefford H, Sharp A, Baker C, Itsara A., et al. Recurrent rearrangements of chromosome 1q21.1 and variable pediatric phenotypes. NEJM 2008, published online Sept 10, 2008. access 10.1056.
13. Nakamoto M, Nalavadi V, Epstein MP, Narayanan U, Bassell GJ, Warren ST. Fragile X mental retardation protein deficiency leads to excessive mGluR5-dependent internalization of AMPA receptors. Proc Natl Acad Sci U S A 2007;104:15537–42.
14. National Library of Medicine (U.S.). List of journals indexed for MEDLINE. In. Bethesda, MD, 2008, U.S. Dept. of Health and Human Services, Public Health Service, National Institutes of Health.