T he most reliable diagnosis in child psy-
chiatry, autism nonetheless remains a 
mystery in many ways. It has no spe-
cific biological marker; a circumstance 
that likely contributes to its attractiveness 
to advocates and zealots, as Paul Offit 
describes in his forceful Autism's False 
Prophets. Persuasion with autism spec-
trum disorders (ASD's) range from non-
verbal individuals with severe intellectual 
disabilities to highly intelligent, articulate 
people who struggle with social expecta-
tions.

Offit is a vaccine researcher and pediatrician at 
the Children's Hospital of Philadelphia and 
the University of Pennsylvania School of 
Medicine (1998, with the now-infamous 
paper by Andrew Wakefield and colleagues that 
reported links between measles-mumps-
rubella (MMR) vaccine and autism (2)). He 
offers an easy-to-read medical thriller 
about the consequences of greed, 
hubris, and intellectual sloppiness. His 
account weaves together cogent comments 
about the dangers of telescoping in 
health care decision-making and 
accounting of scientific-legal debates about 
silicone breast implants and 
facilitated communication in ASD. Sometimes 
tongue-in-cheek (chapter titles include "Mercy 
Rising" and "Mercy Falling"), the book 
vividly portrays the intoxication of enthusiasts 
for vaccination-related hypotheses.

So dramatic was the evidence against 
vaccines that a major well-respected 
production company was going to make 
a movie about it. Everything was com-
ing together. Everything made sense.

This is a tale of heroes (parents and 
scientists willing to stand up to threats and 
accusations) and some unquestionable
villains. It is also the story of lesser culprits who 
may not profit but who cause harm by their 
inconsist-
ten application of scientific standards to their

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own and others' work. A recent 
column (2) by Bernadette 
Healy, a former head of 
the U.S. National Institutes of 
Health, exemplifies this 
problem. Sometimes Offit's com-
ments about particular indi-
viduals seemed a bit unfair. In 
contrast, the financial conflicts 
of interest of some scientists 
and advocates and the failure of others to take 
on these conflicts are much more disturbing.

Surprisingly, Offit does not discuss 
the fact that human decision-making is often 
irrational, especially when it involves 
evaluating 
relative risks and weighing anecdotal 
versus empirical evidence. Anyone forced 
to sign a consent form acknowledging that death 
could be the consequence of routine dental 
work realizes that someone somewhere is 
calculating the risk of ordinary procedures. 
With the present ease of access to unfiltered 
scientific and pseudoscientific data, questions 
of how to help parents evaluate information 
about risk and make rational medical choices 
more go beyond consent forms.

Three types of justification have been 
used to argue that vaccinations (either MMR or 
those that contain thimerosal) cause autism: 
specific hypotheses about effects of mercury 
and the mumps virus on brain function, the 
mediating prevalence of ASDs, and the occur-
cence of regression in autism. Offit carefully 
discusses data discounting the first two justifi-
cations but spares little time on the role of 
regression in explaining many parents' 
beliefs about vaccinations. Yet this is another area 
where science can contribute.

Some children who will 
develop autism show nonspecific 
abnormalities (such as motor, sleeping, or eating 
difficulties) early in life, but autism-specific deficits in use of 
eye contact, facial expres-
sions, and simple social inter-
actions become apparent in ASD in the second 
year of life (3). Some argue that there is a clear, 
specific regressive subtype of ASD. However, 
most children with autism manifest ordinary 
socially. Enacted behaviors at 6 months and do 
not show these behaviors at 24 months, then 
almost all children with ASD experience 
a regression in social—communication skills.

These are children with marked regressions 
and children with subtle losses. Strikingly, 
there is no evidence that any aspect of regres-
sion in ASD is associated with timing of speci-
nation or exposure to thimerosal. The loss of 
social—communication skills is a "red flag" 
for ASD and must be accounted for in explana-
tions of the development of autistic symptoms.

But rather than a "clear regressive phenotype" 
there is a range of patterns, none of which has 
been shown to be related to vaccinations (4).

What next? Offit's call for the application of 
scientific principles to these questions has
NEUROSCIENCE

The Emerging Nature of Nurture
Mirjana Sar

Our minds prefer to deal in dichotomies. We like to see the world as black or white, if only to sharpen issues that demand a decision. The opposite ways in which we frame the world are the stuff of pop psychology as well as of deep dialectics. Thus, Joan Stiles starts The Fundamentals of Brain Development by explaining how developmental psychologists have viewed cognitive development as shaped by either nature or nurture. As the subtitle, Integration: Nature and Nurture, indicates, she aims to bridge this divide. At the outset, she courageously asserts that an understanding of brain development is critical for her project—Courageously, because she is a cognitive scientist (at the University of California, San Diego), not an expert in developmental neuroscience. She ends up taking readers through a surprisingly detailed exposition of brain development and constructing a scholarly synthesis that will inform not only developmental psychology but even all of neuroscience and cognitive science. Halfway through the book, I was wondering whom it was written for. The preface suggests the book is intended for students of cognitive development, and indeed they will find it highly informative. But the heart of the book is really an extended review of the recent literature on brain development. Stiles starts with the gestation and nutrition stages of embryogenesis and continues through the formation of the neural tube, patterning of the neural axis, production, migration, and differentiation of neurons, formation of cortical connections, and shaping of cortical circuits by experience and electrical activity. Stiles precedes this material with a description of the gene—what it is and how it affects gene regulation and expression are evolving rapidly. Indeed, still newer findings on epigenetics and RNA regulation, for example, render even more complex the nature of the gene and even richer the ways in which extrinsic influences shape gene function. The author weaves her description of brain development as a process of progressive commitment of neural elements into a masterful synthesis of innateness, inheritance, development, and plasticity. I learned a great deal from the book, and I suspect other practicing neuroscientists will, too.

Stiles correctly points out that among developmental biologists the debate between nature and nurture has become muddled. We now know that there is no such thing as a gene that acts in isolation and that every gene needs an environment—whether the environment is the presence of molecules made by other genes, signals generated inter- or within the developing nervous system, or electrical activity transmitted from the external world. Thus, the discussion within the field has moved from nature versus nurture to the integration of nature and nurture and even beyond, to the nature of nurture—which kinds of environmental influences can affect gene expression at specific time points of development.

The nature of such environmental influences is a focus of much current research. At the earlier stages of brain development, the mere presence of certain molecules or signals may be sufficient: permissive influences likely suffice to shape gene and protein expression and thus influence brain development. Later on, the influence of the environment may be instructive, so that the specific pattern of signals or of electrical activity shapes brain networks and function.

This is where I suspect the divide that Stiles tries to bridge will likely persist. Nativists will argue that the real issue is not whether an environment is required for brain development but what exactly is required. Indeed, we need to resolve the specific role of learning in development. When and under what conditions is the exact timing of “spike timing dependent plasticity” used by the developing brain? Perhaps the earliest stages of brain development simply require the presence of external signals, and only later, as the neural machinery develops, is the pattern or structure of external information important. Another dilemma arises from the nature of biological information itself. The search for mechanisms of brain development has been illuminated by selective manipulations that alter development. But the changes imposed by such a manipulation may not recapitulate the process of normal development. In the visual cortex, for example, it now appears that the pattern of projections from the two eyes is set up by the targeted early ingrowth of axons from the visual thalamus. Manipulating development by altering activity in one eye alters the pattern of projections, such that the deprived eye occupies less territory while the nondrived eye occupies more. This plasticity, however, is a response of the system to altering the balance of activity, not a process that is necessarily used during development to settle cortical territories. Thus, the processes of plasticity, although available during development, may not be identical to the processes of development per se.

At places, the book is not an easy read. It abounds in sentences such as: “Interestingly, the introduction of fish into posterior regions where it is not normally expressed creates anomalously placed regions that express anterior identity.” This is the language of developmental neurobiologists. But it is in a mark of the level of engagement that Stiles brings and the way she leads readers into the material that we find such conclusions arising naturally in a discussion of cortical patterning (the way in which the developing cerebral cortex gets divided into its cortical areas).

The dichotomies of biology—nature and nurture, constancy and variation, limits and potential—make useful as caricature, are in fact inseparable from one another. As Stiles’s comprehensive overview reminds us, nowhere is this more evident than in human brain development. Fundamentally derived through natural selection, the genes of brain development are impressively environment- and experience-dependent.

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