Formative Experiences

The Interaction of Caregiving, Culture, and Developmental Psychobiology

This interdisciplinary book offers a unique exploration of the formative effects of children's early life experiences, with an emphasis on interactions among neurodevelopmental, behavioral, and cultural dynamics. The authors draw on insights from psychobiological, clinical, and cross-cultural comparative research that maps the robustness of these developmental dynamics across species and societies. Multidisciplinary case studies focus on specific periods of development, or windows of susceptibility, during which caregiving and other cultural practices potentially have a long-lasting impact on brain and behavior. Chapters describe in detail: how social experience interacts with neurodevelopmental disorders; how epigenetic mechanisms mediate the effects of early environment; the interaction of temperament and environmental influences; the implications of early life stress or trauma for mental health and well-being; and the cultural shaping of sexual development and gender identity. The authors also explore key aspects of and common experiences associated with modern childhood, including teasing, bullying, the function of social play, emotional regulation, and management of attention disorders. The final section translates insights from this work into a fresh appraisal of childrearing practices, clinical interventions, and global public health policy that affect the mental health and well-being of children around the world.

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For children and their families, everywhere: their lives, our future. (CMW)

. . . May we as clinicians, researchers, policy makers, teachers, and parents come together to be inspired by and with them [those children and their families, everywhere] to encourage the most wonderful of formative experiences for generations to come! (DSS)

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Foreword

Robert Sapolsky

The field of psychobiology recently lost one of its giants, Seymour "Gig" Levine, who spent a remarkably productive career showing the ways in which early experience shapes the brain and behavior. Although passionately interested in the topic of development, he was realistic enough to admit that it wasn't a subject for everyone – "At some point or other, everyone in our business gets around to doing a development study. After that, either they're hooked forever, or they run away as fast as possible because development's so damn complicated," he once said to me (which I think was meant to taunt me for being in the second category).

Stated in the most low-key manner, the purpose of a volume such as this is not only for the developmental psychobiology obsessives to catch up on the latest work, but also to make such an update readily accessible to the ones who ran away from the subject as fast as possible. Stated more hopefully, this volume can be meant to entice those who did the one-night-stand with the subject into a longer commitment. And stated hegemoniously, it can be meant to convince those who fled that they must start studying development.

But when the current state of developmental psychobiology is considered closely, a conclusion must emerge that speaks to all the other psychobiologists – tough luck, you've got no choice in the matter, you're already studying the development of brain and behavior. And this is because of two facts, namely the plasticity of the brain and the persistence of developmental effects.

The plasticity cannot be overemphasized. This point was captured by the gerontologist Walter Bortz, when asked if his goal was to eliminate aging – "No, I'm not interested in abnormal development." Now a sound

bite like this can be heart-warming, but can easily degenerate into bumper stickers about how today is the first day of the rest of your synapses' lives. What has made the fact of brain development as a life-long process so compelling is that the story is driven by our increasing knowledge of how this actually works. An example of this, relevant to how one must gradually attain maturity, is the extraordinary fact that the frontal cortex does not come fully online until about 25 years of age. This is wildly important. For one thing, this fact informed the decision of the Supreme Court that someone can't be executed for a crime they committed before age 18, because of the immaturity of the brain (although the Court somehow bypassed the fact that something doesn't magically happen to the frontal cortex on the day of your 18th birthday). It gives insight into why schizophrenia so often has a late adolescent onset. It helps explain some of the things your freshman roommate did. And it teaches us that the part of the brain that makes us most uniquely human is the most shaped by environment and least constrained by genetics.

The dictum of development as a life-long process is shown at a more reductive level by the revolution of adult neurogenesis. For the last thousand years, students in Neuro 101 were dutifully taught that the adult brain does not make new neurons. But starting in the 1960s, pioneers like Joseph Altman cried out in the wilderness about how this may not be true, yet it wasn't until the 1990s that the fact of adult neurogenesis was fully demonstrated and widely accepted. The adult brain, particularly the hippocampus, most definitely makes new neurons, and it does so in response to the most interesting circumstances – learning, environmental enrichment, and exercise. Strikingly, such neurogenesis can occur in aged organisms – just another phase of brain development.

So all psychobiologists are ultimately doing development research because of the plasticity of the brain and the fact that it develops throughout the lifetime. The second reason is the persistence of some of the consequences of early experience. A definitive example of this is neonatal handling, a phenomenon first described by Levine, whereby optimal environmental stimulation during the first few weeks of a rat pup's life causes beneficial neurobiological, endocrine, and cognitive changes that persist into adulthood. The changes even last into a rat's old age. And, as a measure of the ethological relevance of this phenomenon, such brain plasticity did not evolve for the benefit of graduate students who like to hold rats. Instead, it turns out to be a surrogate for the effects caused by an optimal style of rodent mothering.

The consequences of early experience can be so persistent as to be multigenerational. Writ small, this concerns the fact that the endocrine changes induced in a female rat by being neonatally stressed will alter the hormonal makeup of her milk when she is a lactating adult, and thereby effect the development of her offspring. Writ larger, this is the truism for both rat and primate that the sort of childhood that individuals experience greatly influences the sort of parents they become. Writ large and pathological, this is the world in which being abused as a child increases the risks of being an abusive parent.

An appreciation of the persistence of the effects of early environmental experience underlines another point, one initially flabbergasting, but ultimately perfectly logical: Environment does not begin at birth. Most obvious is the fact that, say, crack cocaine does not do good things to the fetal brain. Less obvious is the fact that the experiences of a pregnant female will change the hormonal exposure of her fetus, that the endocrine environment of a rodent fetus can even reflect whether the siblings next to her are sisters or brothers. Arguably, the most remarkable example of the persistence of the effects of prenatal environment is the Dutch Hunger Winter phenomenon – people who were fetuses during the catastrophic famine of the winter of 1945 in Nazi-occupied Holland developed "thrifty metabolisms," where the sparseness of fetal nutrition programmed their bodies for a life-long efficiency at storing nutrients. And more than half a century later, the consequences of having been a fetus at that time include a greatly increased risk of obesity, metabolic syndrome, and diabetes.

As noted, an appreciation of the life-long development and plasticity of the brain has been strengthened by uncovering some of the mechanisms underlying such plasticity (e.g., cell cycle regulation in neural progenitor cells). Similarly, mechanisms are being discovered to explain the persistence of some of the effects of early experience. One domain is genetic, e.g., where the likelihood of childhood trauma resulting in adult depression is modulated greatly by polymorphisms in the serotonin transporter gene. Another is epigenetic, e.g., an understanding of how changes in access of transcription factors to promoter elements in DNA can cause persistent silencing of a gene.

So the brain is always developing, and at any given point in life, the brain has been sculpted by all that came before it, even by things long, long before. But this seems to raise a problem. If considered superficially, the elements of persistence and plasticity appear contradictory – on one hand, the consequences of early experience can be huge and so persistent

as to be set in stone for a lifetime. Yet, those stones can turn out to be made of plastic, reshaped by adult experience. Permanent effects that are easily changed. Hmm.

The reconciliation, of course, is that effects aren't necessarily permanent, nor are changes necessarily easy. Such contingencies apply when a salutary developmental effect early in life is derailed by adversity in adulthood. But far more important is the opposite situation, when the pathological consequences of early developmental adversity are lessened by salutary interventions later in life. Except when dealing with the most severe developmental adversity, "persistent" doesn't equal "permanent." But the longer you wait to intervene, the harder it will be to help. And if you never try for recovery and assume that it is already too late to make a change, things that you guess to be permanent will always prove to be.

This insight is quite important when considering a nuts-and-bolts biology issue, such as whether gene methylation induced by a certain mothering style in a rat can be reversed. But it is vastly more important when considering whether long-term consequences can be reversed in humans exposed early in life to abuse or deprivation, to a shortage of calories or of love, or to the corrosive effects of being bathed in alcohol as a fetus or bathed in fear and lessons of helplessness once born. It's swell that all us psychobiologists turn out to be closet developmental psychobiologists. But it's essential that the non-psychobiologists become trained to be as well. The extended plasticity of the brain is the moral imperative to try to make things better, while the persistence is the lesson of what happens if society doesn't make the effort.

Preface

The genesis of this book about development itself has been a developmental process. The structure as well as the source of some of the material derive from a conference held in 2005, entitled "Four Dimensions of Childhood: Brain, Mind, Culture, and Time." Organized and funded by the nonprofit The Foundation for Psychocultural Research (FPR), the meeting was cosponsored by the University of California, Los Angeles, and The Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD, R13HD048149). The conference itself was the product of the vision of FPR founder Robert Lemelson, of discussions by members of the foundation board, and of creative and energetic foundation staff.

The intellectual highlights of the conference drove decisions about formation of the volume. First, we found that the initial focus on advances in developmental neuroscience required expansion to include the equally compelling breakthroughs in epigenetics, genomics, neuroendocrine regulation, and behavioral and social biology. Second, we observed that the interaction among scientists and practitioners around specific cases or findings were particularly revealing. Several sessions at the meeting were organized as case studies, which were then discussed in depth by a panel of researchers from different fields. We found that the diversity of contexts, observations, and perspectives – even within academic disciplines – contributed to a richer understanding of early life experience and its defining moments. Consequently, we set out to identify a complementary set of case studies or research vignettes and then elicited commentary from key

thinkers in other fields. Each set includes a developmental biologist, an anthropologist, and a clinician or development psychobiologist. Thus, the book is organized to combine the strengths of integrative essays with those of analytic case studies.

The manifest value represented in the contents of this volume is due to the efforts of the truly stellar contributors. These important thinkers, practitioners, policy makers, and researchers have generously shared their years of scholarship and experience in the pages of this book. Equally necessary to making the book actually happen are the efforts of several different actors. First, there are the aforementioned visionaries – Robert Lemelson and the Board of the FPR – who fashioned the unique mission and programs of the FPR, conceived of this bold integrative project, and supported its completion. The present book represents yet another FPR accomplishment: it is the second title to appear from the conferences they have hosted, the first being *Understanding Trauma: Integrating Biological, Clinical, and Cultural Perspectives*, edited by Laurence Kirmayer, Robert Lemelson, and Mark Barad.

Second are the movers and shakers, and other organizers. These include Irene Sukwadi, Director of the FPR, who provides the organizational genius that keeps everything going. Then there is Dr. Mamie Wong, who made the graphics in this book happen, among other contributions. Emily Ng, prose stylist with flair, helped with initial editing, followed by two further editors, Enid Pearsons and Linda Thompson, who together helped finalize all contributions to the book. Anyone who has been stymied by a bad or sketchy index will appreciate Erin Hartshorn, our indexer. Isabel Roldos, at Emory, assisted in a crucial stage of organization. Eric Schwartz, formerly of Cambridge University Press and now at Princeton University Press, supported and encouraged us in the early stages of this work. We are deeply indebted to our current editor at Cambridge, Simina Calin, for her astute editorial guidance as well as Christie Polchowski and Jeanie Lee for their editorial assistance on this project.

Three of us editors want to offer special recognition to the fourth among us: A brilliant integrative thinker who at the start of the project preferred to remain modestly behind the scenes, yet without whose creativity and attention to every substantive and practical detail, this book would, in fact, not exist. We honor therefore our colleague and co-editor,

Dr. Constance Cummings of the FPR as an essential driving force, organizing spirit, and intellectual catalyst for the volume before you.

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List of Abbreviations

5-HIAA	5-hydroxyindoleacetic acid (5-HT metabolite)
5-HT	serotonin neurotransmitter
5-HT_{1A}	serotonin receptor
5-HTT	serotonin transporter (gene)
5-HTTLPR	serotonin transporter polymorphism
ABN	arched-back nursing (of rat pups)
ACE	Adverse Childhood Experience Study
ACTH	adrenocorticotropin
ADHD	attention deficit hyperactivity disorder
ADR Ctx	adrenal cortex
ANOVA	analysis of variance
AP	anterior pituitary
APA	American Psychiatric Association
ASB	antisocial behaviors
AVP	vasopressin
BDNF	brain-derived neurotrophic factor
BLA	basolateral complex of the amygdala
BNST	bed nucleus of the stria terminalis
BPD	bipolar disorder
BSQ	Behavioral Style Questionnaire
cAMP	cyclic adenosine monophosphate
CBP	CREB binding protein
CC	corpus callosum
Ce	central nucleus of the amygdala
CG	cytosine-guanine (dinucleotide sequence)
CIFAR	Canadian Institute for Advanced Research

COHORTS	Consortium of Health Outcome Research in Transitioning Societies
CPA	childhood physical abuse
Cr	creatine
CREB	cyclic AMP response element binding protein
CRF	corticotropin-releasing factor
CRH	corticotropin-releasing hormone
(C)SA	contact sexual abuse
CSF	cerebral spinal fluid
CSHCN	children with special health care needs
CSI	Commonwealth of Independent States
CTS	childhood traumatic stress
CV	cerebellar vermis
DHEA	dehydroepiandrosterone
DID	dissociative identity disorder
DNMT	DNA methyltransferase
DS	Down syndrome
DSM	*Diagnostic and Statistical Manual of Mental Disorders*
DTI	diffusion tensor imaging
EBBD	Experience-based Brain and Biological Development (program)
ECCS	Early Childhood Comprehensive Systems Initiative
ECD	early childhood development
ECI	early care and education
ECIC	Early Childhood Investment Corporation
EDI	Early Development Instrument
EEA	environment of evolutionary adaptation
ELN	elastin (gene)
FA	fractional anisotropyy
FKBP5	gene involved in regulating the HPA axis
FL	early focal lesions
FRC	family resource center
GABA	gamma aminobutyric acid
GC	glucocorticoid
GMV	grey matter volume
GR	glucocorticoid receptor
GxE	gene–environment interaction
H	histone (protein)
HAT	histone acetyltransferase
HDAC	histone deacetylase

HDI	Human Development Index
HDM	histone demethylase
HFA	high functioning autism
HMT	histone methyltransferase
HP	hippocampus
HPA	hypothalamic-pituatary-adrenal (axis)
IDEA	Individuals with Disabilities Act
ILF	inferior longitudinal fasciculus
LCHD	Life Course Health Development (approach)
LCN	Salk Institute's Laboratory for Cognitive Neuroscience
LG	licking and grooming (of rat pups)
LI	language impairment
LSCL-33	Limbic System Checklist-33
MAOA	monoamine oxidase (gene)
MAPK	p38 mitogen-activated protein kinase
MDGs	Millenium Development Goals (United Nations)
Me	medial nucleus of the amygdala
mPFC	medial prefrontal cortex
MPQ	Multidimensional Personality Questionnaire
mPSS	PTSD Symptom Scale
NAA	N-acetylaspartate
NAcc	nucleus accumbens
NE	norepinephrine
NMDA	N-methyl-D-aspartate
OFC	orbital frontal cortex
PFC	prefrontal cortex
PFS	perceived financial distress
PK	protein kinase
PP	protein phosphatase
PTSD	posttraumatic stress disorder
PVA	parental verbal abuse
PVN	paraventricular nucleus
RCT	randomized clinical trial
ROR	Reach Out and Read
SAM	S-adenosyl methionine
SERT	serotonin transporter
SES	socioeconomic status
SISQ	Salk Institute Sociability Questionnaire
SNPs	single nucleotide polymorphisms
SNS	sympathetic nervous system

SSBS	social support behaviors scale
T2-RT	brain transverse magnetization relaxation time
TANF	Temporary Assistance to Needy Families
TBSS	Tract-based Spatial Statistics
TD	typically developing (children)
TEI	traumatic events inventory
TNF	tumor necrosis factor
TRP	tryptophan
TSA	HDAC inhibitor
UNICEF	United Nations Children's Fund
VBM	voxel-based morphometry
VBR	voxel-based relaxometry
(W)DV	witnessing domestic violence
WHO	World Health Organization
WM	white matter
WS	Williams syndrome