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189

PROGRESS IN BRAIN RESEARCH

Gene Expression to Neurobiology and Behavior

Human Brain Development and Developmental Disorders

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OLIVER BRADDICK
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ELSEVIER

AMSTERDAM – BOSTON – HEIDELBERG – LONDON – NEW YORK – OXFORD
PARIS – SAN DIEGO – SAN FRANCISCO – SINGAPORE – SYDNEY – TOKYO

Elsevier
Radarweg 29, PO Box 211, 1000 AE Amsterdam, The Netherlands
Linacre House, Jordan Hill, Oxford OX2 8DP, UK
360 Park Avenue South, New York, NY 10010-1710

First edition 2011

Library of Congress Cataloging-in-Publication Data
A catalog record for this book is available from the Library of Congress

British Library Cataloguing in Publication Data
A catalogue record for this book is available from the British Library

ISBN: 978-0-444-53884-0
ISSN: 0079-6123

Printed and bound by CPI Group (UK) Ltd, Croydon, CR0 4YY

Transferred to Digital Print 2011

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Preface

The developing brain: From developmental biology to behavioral disorders and their remediation

Background

The human brain presents the greatest challenge to developmental biology. Its 10^{11} neurons are organized at different scales into large-scale structures, highly specialized nuclei and cortical areas, columns and layers, and microcircuits whose delicate dynamics determine the difference between complex cognitive functions and catastrophic oscillation. Each of these neurons establishes as many as 1000 synaptic connections, some with neighboring neurons but some across the brain over a range of many centimeters. The correct development of this system is required to determine not just a very complex structure but, more importantly, rich, well-integrated, and adaptive behavioral functions. These are as diverse as manipulating the spatial layout of the environment, generating precisely timed sequences of speech, and predicting and managing social interactions.

The development of these systems must depend on the large fraction of the human genome that is expressed in the brain. However, the specification that is required to organize and connect them correctly seems to go way beyond the informational capacity of the genes. The epigenetic processes guided by the external and internal environment must therefore be critical in allowing the developing brain to function. These are central and intrinsically interdisciplinary problems of human development, which can only be understood by a concerted effort of neurobiologists, geneticists, cognitive neuroscientists, neuropsychologists, and pediatric neurologists, with insights from computational modeling of complex, self-organizing systems.

These are not simply questions of profound scientific importance. The complexity of the structures and systems involved means that they are vulnerable to errors in development, caused either by genetic anomalies or by the impact of external conditions such as prenatal anoxia or postnatal stress. The unfolding system of development is dynamic throughout life so that the endpoint in terms of behavior is the result of many interactions along the way. Developmental disorders, such as cerebral palsy, Williams syndrome, Down's syndrome (DS), or Fragile-X syndrome (FXS), autism, or specific language impairment (SLI), prevent a large number of people from participating fully in the demanding economic, social, and personal life of modern communities. They have a heavy lifelong practical, emotional, and economic impact on individuals and their families, not to mention the burden they place on health-care, educational, and social welfare systems.

Key information on the constraints on brain development will come from these conditions that lead to anomalies of brain and cognitive development. In turn, insights on broader questions of brain development will be needed to achieve progress in the identification, treatment, and remediation of these disorders.

This challenge is fundamentally interdisciplinary. Advances in molecular genetics have made it possible to work with animal models of normal and anomalous brain development at every level from gene

expression through brain anatomy to behavior. Neurobiologists have exploited these tools to advance classic questions of the determinants and plasticity of developing brain structure. However, these models will only provide insights into human development if we can adequately characterize human developmental phenotypes at anatomical, functional, and behavioral/cognitive levels throughout development and over time from birth to adulthood. Cognitive and developmental psychologists have applied increasingly sophisticated approaches to these problems. The past decade has seen great advances in integrating behavioral and cognitive analyses with new neuroimaging techniques (such as magnetic resonance imaging (MRI), high-density electroencephalography (EEG), magnetoencephalography (MEG)) that make possible noninvasive measurements of the human brain in unprecedented detail, and these methods are starting to be applied to developing children. We are also at the beginning of using these methods of developmental cognitive neuroscience to define phenotypes at various levels, which can be linked to genetic variation.

Neurobiologists and geneticists working in these areas will need to understand theories, methods, and insights in human cognitive development. Conversely, cognitive and developmental psychologists and neuroscientists will need to appreciate the possibilities, limitations, and issues of interpretation in the new biological technologies. But ultimately, the opportunities to exploit scientific advances in understanding developmental disorders can only be realized through intellectual and practical interchange with the medical specialists in neuropsychiatry and pediatric neurology who are responsible for the care of the children and families concerned.

The European Research Conference

With the opportunities and challenges of this multifaceted problem in mind, we convened a research conference under the auspices of the European Science Foundation in Sant Feliu de Guixols, Catalonia, Spain, in September 2009. Leading scientists were invited to present state-of-the-art work and reviews from across this range of relevant disciplines. The aim was to allow the cross-disciplinary links to develop both among the invited speakers and in the minds of the younger scientists who participated in the audience and presented posters of their current research. In this emerging linkage, the typical course of development should be used to help characterize and understand neurodevelopmental disorders, and conversely, disorders should throw light on how the process of typical development operates. We hope that the present volume will bring this perspective to a wider audience.

We are particularly grateful that some authors, who did not participate in the original meeting, were nonetheless willing to make contributions to this volume and thereby enhance its scope and comprehensiveness. Among these, Antonello Mallamaci has provided a strong background in the detailed cellular and molecular events that guide the development of the large-scale structure of the brain. Rhonda Booth, Gregory Wallace, and Francesca Happé fill an important niche in considering the relationship between the symptomatology of autism spectrum disorder (ASD) and anomalies of cerebral connectivity in this condition.

Introductory chapters

We open this volume with some chapters that explain the broad theoretical issues linking the elements of our title—gene expression, neurobiology, and behavior. Joan Stiles gives us a brief overview of the

neurobiology of brain development, introducing concepts and processes which are developed in more detail in some of the later chapters such as those by Mallamaci and Giorgio Innocenti. She reviews ways in which this developmental process is modulated and can be redirected by the pattern of sensory input to the brain. The chapter emphasizes the importance of understanding brain development as a process over time, in which the effect of influences (genetic or environmental) at time T_3 depends on what has been laid down in the sequence of events from time T_1 to time T_2. This sequential process of interaction supersedes the naïve dichotomy between "nature" and "nurture," which dominated much psychological debate in the past 100 years.

Tessa Dekker and Annette Karmiloff-Smith develop this approach in the context of the widespread "modular" view of brain and cognition. They critique the idea that specialized modules in the brain are the starting point of cognitive development and argue for a "neuroconstructivist" approach in which initial functional biases are the starting point for an increasingly domain-specific specialization of brain structures in the course of development. On this basis, they critically examine some of the assumptions that may lead to developmental disorders being considered as the impairment of specific modules and the potential analytical pitfalls in comparing patterns of activity in the brain at different stages of development. The ideas of the related "interactive specialization" approach are relevant to a number of the chapters in this volume (e.g., those by Peter Klaver, Valentine Marcar, and Ernst Martin; Oliver Braddick, Janette Atkinson, and John Wattam-Bell; Gaia Scerif and Ann Steele; and Francesca Simion, Elisa Di Giorgio, Irene Leo, and Lara Bardi).

As we focus on the more specific content of subsequent chapters, it is important to see these as a matrix of several intersecting factors: our authors use particular methodologies, they are concerned with particular developmental disorders, and they focus on particular aspects of cognitive ability and disability.

Techniques

The chapters in this volume illustrate much of the wide-ranging armory of techniques which has become available to neuroscience in recent decades and which is being increasingly applied to development. A number of chapters benefit from the powerful tools of molecular genetics; in particular, their application in animal models of anatomical development is at the core of the work described by Antonello Mallamaci. The chapters by Terry Jernigan, William Baaré, Joan Stiles and Kathrine Skak Madsen, and Kate Watkins illustrate the potential scope for relating individuals' genetic characterization to variations in their brain structure, and those by Watkins and by Mayada Elsabbagh, Karla Holmboe, Teodora Gliga, Evelyne Mercure, Kristelle Hudry, Tony Charman, Simon Baron-Cohen, Patrick Bolton, Mark Johnson, and the BASIS Team in relating genetic to cognitive or behavioral variations. It should be noted that genetically based disorders, and polymorphisms found in the typically developing population, have both proved informative in analyzing these gene–brain-behavior relationships.

The range of techniques for probing the brain using MRI is well represented here, making clear that these are increasingly available for use with developing children, although their application to infants is still challenging. The classical use of MRI to visualize brain structure has been applied to neonates, allowing perinatal brain injury to be related to functional measures (see examples in chapters by Braddick et al. and Giovanni Cioni, Giulia D'Acunto, and Andrea Guzzetta). Structural studies of development have become increasingly quantitative, with the use of voxel-based morphometry to characterize the distribution of white and gray matter in the brain (see the chapters by Jernigan et al. and Watkins),

measurements of cortical thickness in the course of development (Jernigan et al. and Klaver et al.), and diffusion tensor imaging (DTI) to assess the organization of white matter tracts and to track these to discover the interconnections of cortical areas (chapters by Klaver et al., Jernigan et al., and Watkins).

Much of the excitement in adult MRI studies has come from functional MRI (fMRI) studies using the BOLD (blood oxygen level-dependent) response to reveal patterns of local brain activation in individuals when they carry out cognitive operations. This approach is reviewed here with examples in the chapter by Klaver et al. and alluded to in many other chapters; published experiments on face processing, visuomotor function, and language processing show that the problems of fMRI with young children are gradually yielding to patient and persistent experimenters. We may hope that technical advances in MRI scanning and analysis will make this powerful method more accessible as a developmental tool in the years ahead. One specific application of fMRI is to use patterns of temporal correlation in activity to infer patterns of connectivity, particularly the "resting state" or "default mode" of brain activity in the absence of a specific task. Such inferences of connectivity in development appear in the chapters by Booth et al. and by Klaver et al.

A more practical route to probe brain activity in the youngest children is to record event-related potentials (ERPs) from sensors on the scalp. This method has yielded much of our information about brain function in the first years of life, as exemplified here by the chapters by Braddick et al., Cioni et al., and Elsabbagh et al. With the use of high-density sensor arrays, it can provide a form of functional brain imaging, carrying a wealth of information about the time course of processing.

The use of new technologies to study the development of cognitive brain function should not be allowed to overshadow the fact that such work and behavioral studies depend totally on the creative and careful application of cognitive task design to ask specific questions about children's capabilities, in a well-controlled, age-appropriate way, and the rigorous application of methods of data analysis. Cognitive and developmental psychologists have been refining these approaches for many years: examples of such creative experimentation and analysis appear in almost every chapter in this volume.

Brain development

The admirable work of anatomists at the end of the nineteenth century, particularly Brodmann (published in 1909) and Campbell (in 1905) demonstrated differences in the cytoarchitecture and myeloarchitecture of cerebral cortical sectors, leading to the identification of cortical areas. Subsequent work, continuing to this date, has established strong correlations between structural and functional properties of cortical areas using a variety of techniques in animal models and in humans. The question tormenting the curious biologist was "what causes the formation of cortical areas in development?" Mallamaci's chapter provides a summary of a recent debate on this issue. More important, it discloses the up-to-date landscape of the fantastically complex (and we are only at the beginning) network of causal-molecular/genetic interactions which lead to the emergence of what can be considered the basis of cortical organization.

Mallamaci presents basic research from animal models, in which genetic manipulations have allowed researchers to unpick the molecular mechanisms guiding these developmental pathways. However, it does not require much imagination to see the longer-term possibilities for understanding human developmental disorders in which genetic anomalies (whether point mutations, deletions, number of repeats, or other rearrangements of the genome) may divert or distort these pathways, leading to a change in the balance or organization of cortical development.

"Environment" in the examples expounded by Mallamaci consists primarily of the internal environment of the developing brain—where the topography of proteins laid out at one stage of the process triggers and modulates the expression of genes defining cortical specialization at a later stage, and patterns of afferent activity guide the differentiation of cortical structure. However, this internal environment is coupled to the pre- and postnatal *external* environment of the developing organism. Such coupling occurs (a) because the chemical environment is determined by events such as anoxia, (b) because internal hormonal effects are coupled to external stressors and to emotionally significant stimuli such as parental grooming, and (c) connectivity is organized by the structure of sensory inputs which in turn is partly determined by feedback loops from the activity of the developing individual. Thus, accounts such as Mallamaci's will in due course become integrated into an account of the recurrent linkages between the molecular architectures produced by gene expression; the pattern of cerebral connectivity; the external chemical, sensory, and social environment; and the internal chemical environment which bathes the nervous system. To quote Joan Stiles' chapter, "the boundaries between what is internal to the organism and what is external are fluid."

The development of long-range connections in the brain has most often been discussed, as in the chapters by Stiles and Mallamaci, in terms of their finding appropriate targets. However, the properties of the connecting axons are also important, especially since they determine the time pattern in which neural information arrives at its destination, a pattern which is critical for some processes such as motion perception (see the chapter by Braddick et al.) and is also important for development, given the role of coincident timing in mechanisms such as the Hebb synapse. The chapter by Giorgio Innocenti focuses on the differentiation of axon types, particularly in their thickness which determines the speed of long-range neural information transmission. Innocenti's chapter is distinctive in taking an evolutionary perspective, using the distribution of axon diameters in different cortical areas and in different primates, macaque, chimpanzee, and human. It points out that the environment exerts selective pressure both in development and in evolution. The fact that both processes seem to act to increase the diversity of axon diameters (and hence the variance of transmission times) raises the question of how and why such variance is adaptive, a challenge for the modeling of cortical circuits but a feature which Innocenti suggests may expand the dynamic range of oscillatory neural interactions and improve the stability of brain activity. Conversely, disruption of this diversity in developmental disorders might conceivably lead to decreased stability, with knock-on effects on functional development.

Jernigan et al. turn to direct neuroimaging evidence of how the human brain changes during childhood. It is now clear that this is a protracted process, lasting through adolescence into young adulthood. It is reflected, counterintuitively, in the progressive thinning of the cortex, which may reflect the increasing myelination and organization of white matter fiber tracts revealed by DTI. The studies reviewed by Jernigan et al. have now gone beyond overall description of population trends in anatomical development, to show the association of local white and gray matter changes with individual measures of intelligence and memory, with task-specific training in reading and sensory-motor skills, and with the independent actions of specific genetic variants. Hormonal levels around puberty also have an important impact in specific structural measures. Overall, this kind of work promises to reveal the neurobiological pathways through which specific genes underlie psychometric variability and the ways in which environmental stimulation intervenes to modulate these pathways.

Specific, distinct pathways from genes through brain systems to behavioral variation are presented in the chapter by Adele Diamond. She explains how the specific neurochemistry of prefrontal cortex determines how that brain area responds to genetic polymorphisms and mutations that impact on the dopamine (DA) system. In turn, these variations affect the development of executive function, critical in the "inattentive"

form of attention-deficit disorder. A different genetic–neurochemical pathway, through the DA system in the striatum, is responsible for the "hyperactive" form. Thus neurobiology can help us to understand how developmental disorders should be properly categorized and, critically, guide therapy.

Environmental impact and plasticity

The chapters by Cioni et al. and by Jörg Bock, Gerd Poeggel, and Katharina Braun provide evidence on how external stimulation can affect the direction of brain development in the neonatal period. Cioni et al. first discuss the plasticity shown in the infant brain in functional recovery from perinatal brain injury, in particular, the transfer of language and sensory-motor functions between hemispheres. Interhemispheric and intrahemispheric transfer of function appear to show different potential in different systems—while the sources of this difference are not fully understood, they have strong implications for choosing the most effective early therapeutic interventions and their timing. More global interventions may also be important as neuroprotective strategies in the developing brain. Animal models have shown that enriching impoverished environments through social housing and providing opportunities for physical manipulation and exploration enhances brain growth and connectivity and that intensive maternal care of rat pups elicits neurotrophic factors that enhance cortical development and reduce cell death. These models have promoted the use of massage for at-risk preterm babies in neonatal intensive care units, which has been shown to have analogous effects on neurochemistry and on the development of the EEG.

The purpose of research on developmental disorders and their basis in the brain must be to enable children to reverse or minimize the impact of these disorders on their lives. The approaches discussed by Cioni et al. and Bock et al. help toward this end by interventions in early infancy. However, functions of behavioral and cognitive self-regulation are key for effective social living and achieving life goals. These key functions develop at a later stage and are exemplified in tasks when children work together on tasks which require sustained focus and planning to achieve a goal. Cognitive, affective, and social aspects of behavior are integrated in such tasks. The chapter by Diamond describes a new approach of providing kindergarten children, working and playing together, with "tools for the mind," aiming to give them the means to overcome attentional disorders and become fulfilled members of a purposeful society.

The work reported by Bock et al. illustrates the converse effect, that separation of neonatal animals from parental care and litter mates acts as a stressor which downregulates brain activity in many areas, and if repeated leads to chronic metabolic hypofunction of the brain and atypical behavioral patterns. Both stress and environmental enhancement effects show that external stimulation can radically modify the way in which genetic programs are expressed in brain development. These effects imply that there are profound therapeutic possibilities of stimulation for infants whose neural and behavioral development is at risk through the challenges of premature birth and hypoxia, or through the stressors of neglect and deprivation. The work of Bock et al. also indicates that pharmacological interventions may be able to correct the downregulation and ameliorate its behavioral consequences.

Disorders

Research attention has focused on particular developmental disorders in part because of their impact on the lives and families of those affected, and partly for their scientific potential in revealing processes of development.

WS has attracted much attention; it results from a well-defined and intensively explored genetic deletion and has a highly uneven and characteristic profile of cognitive impairment, notably in the visuospatial domain. This has raised the hope that WS will be revealing about how features of the genotype are translated into specific aspects of cognitive processing. The chapter by Janette Atkinson and Oliver Braddick discusses the pattern of WS performance in terms of the brain mechanisms for vision, action, and attention, considering the hypothesis that the dorsal stream of visuospatial processing is especially vulnerable. This vulnerability, it turns out, is revealed in many different developmental disorders. Accounts of the genetic effects in WS must therefore recognize that while the overall profile of this disorder is unique, it reflects effects on pathways of brain development that are involved in a much wider range of disorders. Processes of attention are closely associated with the dorsal stream and also with frontal executive function. Atkinson and Braddick introduce a new testing battery designed to partition attentional subsystems in children of a young mental age, which reveals that WS and DS have their own characteristic profiles of attentional strengths and weaknesses, over and above the effects of their overall cognitive delay.

FXS is another disorder with a well-specified genetic origin (excessive repeats of a specific three-nucleotide sequence, causing failure to express the FMR1 protein) and a characteristic cognitive/behavioral profile. The chapter by Gaia Scerif and Ann Steele uses the component structure of attention (in a similar approach to Atkinson and Braddick) to compare the developmental trajectories in FX, WS, and DS. They find not only that these conditions differ in their pattern of abilities but also how these patterns change in development. These attentional skills clearly have an impact on the developmental course of other abilities requiring learning and memory; but the syndromes also diverge in how far deficits seen in childhood have their adult counterparts, suggesting that the availability or otherwise of compensatory strategies may be a key characteristic of anomalous developmental trajectories.

Autism, and the broader category of *autistic spectrum disorder*, is one of the most intensively investigated disorders, because of its relatively high incidence, the severity of its impact in some cases, and again its specific profile which may in some cases allow high intellectual capacities to coexist with crippling failures of normal social interaction. The chapter by Rhonda Booth, Gregory Wallace, and Francesca Happé provides an overview of ASD, considering whether the classic diagnostic triad (social withdrawal, communicative impairment, and rigid/repetitive behavior) is in fact unitary. They present evidence that while there are associations between these elements, each of them can be present without the other two. Thus the search for neurodevelopmental pathways should consider the elements of the triad separately as well as together. Booth et al. pursue the hypothesis that ASD is associated with increased early brain growth but impaired cerebral connectivity, especially between the hemispheres. They test whether a distinct neurodevelopmental disorder, agenesis of the corpus callosum, may be a model for some aspects of the ASD triad; they find some commonalities in social and communicative problems, but no evidence for the cognitive rigidity and "detail-focused processing bias." A parallel analysis of other aspects of the triad will be required to understand how these components interact in the developmental trajectory of ASD.

Autism is typically diagnosed in the second or third year of life, but there is a general belief that it has congenital roots. Elsabbagh et al. studied 9 month olds who, as siblings of diagnosed cases, were at risk for ASD and found that they differed from controls in their ERP responses to eye contact and in a proposed measure of attentional flexibility, the "freeze-frame" task. This, and other studies reviewed by Elsabbagh et al., suggests that infants may show perceptual and cognitive biases which reflect the developmental seeds of autism. However, the critical data for tracking this developmental trajectory are to compare the results in infancy with the later emergence of definitive ASD characteristics. As the authors

point out, diagnostic information from larger groups followed up over a longer period will be required to validate the predictive value of infant indicators and to determine whether an ASD outcome depends on the convergence of multiple developmental risk factors.

The idea that an aversion to eye contact is an early stage and perhaps a key mediator of the development of ASD has been an influential one. The chapter by Terje Falck-Ytter and Claes von Hofsten discusses and reevaluates this idea. They review in detail evidence that ASD individuals, compared to controls, when confronted with a face image, look less at the eye area and more at the mouth. While this result seems to have widespread support in adult ASD individuals, the evidence for such a pattern of bias in children under 12 years was found to be weak and fragmentary. The results they review show more reliable excess looking to the mouth, but not reduced looking to the eyes, and that the balance of mouth:eye fixations reduces in typical development but not in ASD. They suggest that this pattern reflects a more prolonged use of visual mouth information for language acquisition in ASD. These results mean that while poor eye contact and deficits in the use of social information are both features of adult ASD, the direction of causality between them in the developmental pathway for the disorder must be questioned.

Perinatal brain injury

Recent decades have seen enormous improvements in obstetrics and the care of the newborn, leading to increased survival, particularly of infants born very prematurely. However, this means that brain damage, resulting from hypoxia and ischemia in the newborn, remains among the developmental problems with the greatest individual and societal impact. Cioni et al.'s chapter provides an overview of the risks and mechanisms of perinatal brain damage, and the plasticity of the developing brain which means that the functional impact of these injuries may fortunately be much less than the equivalent lesion in adulthood. Braddick et al. report work with this group, showing that visual brain responses can be an early and sensitive indicator of the overall effect of perinatal brain damage, and reveal the differential vulnerability of different brain systems, notably the dorsal stream involved in visual motion processing. Laura Bosch describes the impact of preterm birth on some aspects of language acquisition.

Specific cognitive impairments

"Specific learning disabilities" (SLDs), where one cognitive domain is impaired in individuals whose development and abilities are otherwise typical, are the subject of intense scientific and public interest. Proper coverage of SLDs such as dyslexia and dyscalculia would have made the ESF Research Conference, and this volume, impossibly large. However, these disabilities must surely be ultimately understood in terms of genetic dispositions interacting with environmental influences and demands, acting through pathways in the developing structure and organization of the brain, and many researchers are pursuing this route. One example which may serve as a model is the investigation of developmental impairments of language, described in the chapter by Kate Watkins. The discovery of a family with a pedigree of SLI has enabled the links to be established between mutation of a specific gene, atypical brain structure, and the pattern of behavioral impairment. It is instructive that the fundamental impairment appears to be in the organization and control of programs for delicately timed face and mouth movements. Disorganization of the basic motor machinery required for speech production must lead to a cascade of

developmental effects, some of which, for example, in the mastery of grammatical morphology, may seem to be much more linguistically abstract. This is a lesson for all who are trying to understand specific learning difficulties and other syndromes: the developmental roots of a problem may lie in much lower-level mechanisms than the difficulties which are most evident at a later stage. This is also related to a theme of the chapter by Atkinson and Braddick, in their suggestion that early attentional deficits, viewed as difficulties in shifting focus in WS, coupled with motion processing deficits, may be the developmental starting point of many of the later spatial difficulties.

Visual processing

Two of our chapters focus on visual processing, an area where animal and human neuroscience have given us a uniquely detailed understanding of the functional networks involved. Both Braddick et al. and Klaver et al. give particular attention to the network of areas involved in global motion processing. Work described by Braddick et al. show that this network undergoes substantial reorganization between infancy and adulthood, and the MRI studies reviewed by Klaver et al. find developmental changes between 5 and 7 year olds and adults in the balance of lower- and higher-level structures activated by displays such as structure from motion. Overall, these studies make clear that an apparently similar ability to detect global motion may be subserved at different ages by differently organized networks. Both chapters also make it clear that the relative rates of development of dorsal and ventral streams have a complex history; any statements about one maturing faster than the other must be qualified according to what stage of development, at what level of the system, is being described. These issues may serve as sources of caution for the study of the developmental trajectory in systems whose organization is less well understood.

Social perception

A specialized aspect of visual processing is our ability to register information about other members of our species—individual identity, emotional state, communicative intent—from their faces. This has been of great interest to developmental neuroscientists for several reasons. First, there is much evidence for the role of a specialized neural system, including the "fusiform face area," in processing visual face information. Second, as discussed above, anomalies in attending to and registering facial information are a characteristic of ASD, and possibly one with an important role in the development of the disorder. Third, sensitivity to faces is apparent at or soon after birth and presents a challenge to neurobiological theories on the emergence of specialized cortical properties. This last question is the focus of the chapter by Simion et al. They show how the newborn's attention to faces can be accounted for by initial biases to some simple geometrical image properties, such as relative contrast density in the upper and lower parts of the image. On this view, relatively coarse-tuned biases in attention can determine the early input to the system, and so provide stimulation which refines the tuning and ultimately leads to a highly specific neural system. They present evidence that the neural systems that make us exquisitely sensitive to biological patterns of motion may be refined by a similar process. Such processes by which broad biases guide the acquisition of information, and so provide the basis for high selectivity in a self-organizing system, may prove to be fruitful models in many domains of cognitive development and lead to understanding of how patterns of developmental disorder emerge.

Language

The organization of a specialized perceptual system deriving from broad biases may have its counterpart in the development of the language system. Language is complicated by the way it combines receptive and productive aspects; as the discussion of Watkins' chapter above makes clear, a disruption on one side of this reception–production cycle may have far-reaching knock-on effects on the other. However, in all aspects of language development, reception precedes production. The chapter by Bosch illustrates that there are many levels at which learning processes have to extract information from speech input: the detection of individual phonetic features characteristic of the particular native language environment is acquired early and robustly, but the partition of the speech stream into distinct words, based on statistical and temporal properties, is more demanding and more subject to impairment by the problems associated with preterm birth. As with vision, the detail with which we can characterize language structure at several different levels may make this area one which suggests models and provides sensitive tests for broader questions about cumulative developmental processes.

Concluding remarks

Inevitably, the constraints of time and commitments mean that not all the invited speakers were available to contribute chapters to this volume. The meeting in Sant Feliu benefited greatly from contributions from Lucy Osborne from Toronto and Tassabehji from Manchester discussing gene expression in developmental brain disorders (see *Am J Med Genet C Semin Med Genet*, 2010, and *Eur J Hum Genet*, 2006) and Ghislaine Dehaene-Lambertz from Paris presenting research on the neural basis of infants' language abilities (see *Trends in Neuroscience,* 2006).

Feedback about the meeting was very positive from both junior and senior researchers alike across all the represented disciplines. We hope that readers of this volume will be inspired by perspectives presented in these chapters and that through their efforts we might gain better understanding and funding for this interdisciplinary approach in the future.

Acknowledgments

In addition to the vital support from the European Science Foundation's Research Conferences Scheme, the meeting from which this volume has developed was aided by generous support from the Guarantors of Brain, and the *Comissionat per a Universitats i Recerca* of the Generalitat de Catalunya. Individual contributors were also aided by their own research grant support as cited in the acknowledgments of their contributions.

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