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RESEARCH ARTICLES SHARED BY DR ROBERT MELILLO

Name | Childhood Neurology | Date

One hundred million years of interhemispheric communication: the history of the corpus callosum

F. Aboitiz and
J. Montiel

Departamento de Psiquiatría y Centro de Investigaciones Médicas,
Facultad de Medicina, Pontificia Universidad Católica de Chile,
and Millenium Nucleus for Integrative Neuroscience, Santiago, Chile

Abstract

Correspondence

F. Aboitiz
Departamento de Psiquiatría,
Facultad de Medicina
Pontificia Universidad Católica
Marcoleta 387, 2º piso
Casilla 114-D
Santiago 1
Chile
Fax: +56-2-665-1951
E-mail: faboitiz@med.puc.cl

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Analysis of regional corpus callosum fiber composition reveals that callosal regions connecting primary and secondary sensory areas tend to have higher proportions of coarse-diameter, highly myelinated fibers than callosal regions connecting so-called higher-order areas. This suggests that in primary/secondary sensory areas there are strong timing constraints for interhemispheric communication, which may be related to the process of midline fusion of the two sensory hemifields across the hemispheres. We postulate that the evolutionary origin of the corpus callosum in placental mammals is related to the mechanism of midline fusion in the sensory cortices, which only in mammals receive a topographically organized representation of the sensory surfaces. The early corpus callosum may have also served as a substrate for growth of fibers connecting higher-order areas, which possibly participated in the propagation of neuronal ensembles of synchronized activity between the hemispheres. However, as brains became much larger, the increasingly longer interhemispheric distance may have worked as a constraint for efficient callosal transmission. Callosal fiber composition tends to be quite uniform across species with different brain sizes, suggesting that the delay in callosal transmission is longer in bigger brains. There is only a small subset of large-diameter callosal fibers whose size increases with increasing interhemispheric distance. These limitations in interhemispheric connectivity may have favored the development of brain lateralization in some species like humans.

Key words

- Commissures
- Evolution
- Interhemispheric communication
- Lateralization
- Synchronization



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Lateral Asymmetries in Infancy: Implications for the Development of the Hemispheres

COLWYN TREVARTHEN

*Edinburgh Centre for Research in Child Development, Department of Psychology,
The University of Edinburgh, U.K.*

TREVARTHEN, C., *Lateral asymmetries in infancy: implications for the development of the hemispheres*. NEUROSCI BIOBEHAV REV 20 (4)571–586, 1996.—Cerebral asymmetry of cognitive processing of stimulus information is commonly viewed as a neocortical phenomenon. However, a number of lines of evidence give innate asymmetry of brainstem motivating systems, which anticipate experience, a key role.

Spontaneous asymmetries of gesture and emotion can be observed in infants, who entirely lack language and visuo-constructive skills. Motives for communication in early life may direct subsequent development of complementary cognitive systems in left and right hemispheres. In split-brain monkeys, lateralized motive sets, intentions for manipulation by one hand, can determine which hemisphere will see and learn. Evolutionary antecedents of cerebral asymmetry appear to affect motivation, social signalling and bimanual coordination, with secondary effects in perceptual processing and learning.

The hemispheres of adult humans differ in links with neurochemical systems that regulate motor initiatives, exploration and attention, and the approach/withdrawal balance in social encounters. Asymmetries in emotional and communicative behaviour in infancy support evidence that an Intrinsic Motive Formation emerging in the embryo human brain stem regulates asymmetries in development and in functioning of the cerebral cortex. Copyright © 1996 Elsevier Science Ltd.

The right brain hemisphere is dominant in human infants

C. Chiron,^{1,2} I. Jambaque,² R. Nabbout,¹ R. Lounes,³ A. Syrota¹ and O. Dulac²

¹Hospital F. Joliot, Department of Medical Research, Atomic Energy Commission, Orsay, ²INSERM Unit 29 and Neuropediatric Department, Hospital Saint Vincent de Paul and University Rene Descartes and ³University Paris V, Medical statistic laboratory, UA CNRS 1323, Paris, France

Correspondence to: Catherine Chiron, Service de Neuropediatrie, Hopital Saint Vincent de Paul, 82 avenue Denfert Rochereau, 75674 Paris cedex 14, France

Summary

The development of functional brain asymmetry during childhood is confirmed by changes in cerebral blood flow measured at rest using dynamic single photon emission computed tomography. Between 1 and 3 years of age, the blood flow shows a right hemispheric predominance, mainly due to the activity in the posterior associative area.

Asymmetry shifts to the left after 3 years. The subsequent time course of changes appear to follow the emergence of functions localized initially on the right, but later on the left hemisphere (i.e. visuospatial and later language abilities). These findings support the hypothesis that, in man, the right hemisphere develops its functions earlier than the left.



Autistic Spectrum Disorders as Functional Disconnection Syndrome

Robert Melillo¹ and Gerry Leisman^{1,2}

Reviews in the Neurosciences 2009 [In Press] © Freund Publishing Co.

Abstract

We outline in this paper the basis of how functional disconnection with reduced activity and coherence in the right hemisphere would explain all of the symptoms of autistic spectrum disorder as well as the observed increases in sympathetic activation. If the problem of autistic spectrum disorder is primarily one of desynchronization and ineffective interhemispheric communication, then the best way to address the symptoms is to improve coordination between areas of the brain. To do that the best approach would include multimodal therapeutics that would include a combination of somatosensory, cognitive, behavioral, and biochemical interventions all directed at improving overall health, reducing inflammation and increasing right hemisphere activity to the level that it becomes temporally coherent with the left hemisphere. We hypothesize that the unilateral increased hemispheric stimulation has the effect of increasing the temporal oscillations within the thalamocortical pathways bringing it closer to the oscillation rate of the adequately functioning hemisphere. We propose that increasing the baseline oscillation speed of one entire hemisphere will enhance the coordination and coherence between the two hemispheres allowing for enhanced motor and cognitive binding.

KEYWORDS: epigenetic, ADHD, Asperger's, autism, epigenetic, functional disconnection, dopamine systems, gamma oscillations, Hemisphericity, dysautonomia

The Early Development of the Autonomic Nervous System Provides a Neural Platform for Social Behaviour: A Polyvagal Perspective

Stephen W. Porges[✉] and Senta A. Furman

Brain-Body Center, Department of Psychiatry, University of Illinois at Chicago, Chicago, IL, USA

We present a biobehavioural model that explains the neurobiological mechanisms through which measures of vagal regulation of the heart (e.g. respiratory sinus arrhythmia) are related to infant self-regulatory and social engagement skills. The model describes the sequential development of the neural structures that provide a newborn infant with the ability to regulate physiological state in response to a dynamically changing postpartum environment. Initially, the newborn uses primitive brainstem-visceral circuits via ingestive behaviours as the primary mechanism to regulate physiological state. However, as cortical regulation of the brainstem improves during the first year of life, reciprocal social behaviour displaces feeding as the primary regulator of physiological state. The model emphasizes two sequential phases in neurophysiological development as the fetus transitions to postpartum biological and social challenges: (1) the development of the myelinated vagal system during the last trimester and (2) the development of cortical regulation of the brainstem areas regulating the vagus during the first year postpartum.

PRIMITIVE REFLEXES AND THEIR RELATIONSHIP TO DELAYED CORTICAL MATURATION, UNDER CONNECTIVITY AND FUNCTIONAL DISCONNECTION IN CHILDHOOD NEUROBEHAVIORAL DISORDERS

• **Robert Melillo***

- F. R. Carrick Institute for Clinical Ergonomics,
- Rehabilitation, and Applied Neurosciences
- Garden City, New York USA

Infantile Reflexes Gone Astray in Autism

Philip Teitelbaum (1), Osnat B. Teitelbaum (1), Joshua Fryman (2), and Ralph Maurer (3).

(1) Department of Psychology, Gainesville, FL 32611

(2) Computer Science Department, Georgia Institute of Technology, Atlanta, GA

(3) Department of Child Psychiatry, University of Florida Medical School, Gainesville, FL 32610

Abstract. *In the cases presented in this paper plus others we hypothesize that movement disturbances in infants can be interpreted as reflexes gone astray and may be early indicators for a diagnosis of autism. In the children reviewed some reflexes persist too long in infancy, whereas others first appear much later than they should. The asymmetrical tonic neck reflex is one reflex that may persist too long in autism. Head-verticalization in response to body tilt is a reflex that does not appear when it should in a subgroup of autistic-to-be infants. We suggest that it may be used by pediatricians to screen for neurological damage that may be a marker for a subgroup of autistic-to-be children, especially in families where there is a history of autism.*

Introduction

In our earlier work (Teitelbaum, 1998) we showed that infants destined to become autistic showed a characteristic cluster of disturbances in movement patterns detectable by our methods as early as 4-6 months of age. To do this, we used Eshkol-Wachman Movement Analysis (EWMN) (Eshkol, 1958) in conjunction with laser disc still-frame analysis. Through the cases presented plus others we suggest that the movement disturbances in infancy in autism can be understood as reflexes gone astray in infancy. In the present paper, we will re-analyze some of these movement disturbances in terms of infantile reflexes.

Dysregulation of the right brain: a fundamental mechanism of traumatic attachment and the psychopathogenesis of posttraumatic stress disorder

Allan N. Schore

Objective: This review integrates recent advances in attachment theory, affective neuroscience, developmental stress research, and infant psychiatry in order to delineate the developmental precursors of posttraumatic stress disorder.

Method: Existing attachment, stress physiology, trauma, and neuroscience literatures were collected using *Index Medicus/Medline* and *Psychological Abstracts*. This converging interdisciplinary data was used as a theoretical base for modelling the effects of early relational trauma on the developing central and autonomic nervous system activities that drive attachment functions.

Results: Current trends that integrate neuropsychiatry, infant psychiatry, and clinical psychiatry are generating more powerful models of the early genesis of a predisposition to psychiatric disorders, including PTSD. Data are presented which suggest that traumatic attachments, expressed in episodes of hyperarousal and dissociation, are imprinted into the developing limbic and autonomic nervous systems of the early maturing right brain. These enduring structural changes lead to the inefficient stress coping mechanisms that lie at the core of infant, child, and adult posttraumatic stress disorders.

Conclusions: Disorganised-disoriented insecure attachment, a pattern common in infants abused in the first 2 years of life, is psychologically manifest as an inability to generate a coherent strategy for coping with relational stress. Early abuse negatively impacts the developmental trajectory of the right brain, dominant for attachment, affect regulation, and stress modulation, thereby setting a template for the coping deficits of both mind and body that characterise PTSD symptomatology. These data suggest that early intervention programs can significantly alter the intergenerational transmission of posttraumatic stress disorders.

Key words: attachment, child abuse, dissociation, right brain, trauma.

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Dr.



Cognitive-motor interactions of the basal ganglia in development

Gerry Leisman^{1,2,3,4*}, Orit Braun-Benjamin^{1,2} and Robert Melillo^{1,3,5}

¹ The National Institute for Brain and Rehabilitation Sciences, Nazareth, Israel

² Department of Mechanical Engineering, ORT-Braude College of Engineering, Karmiel, Israel

³ FR. Carrick Institute for Clinical Ergonomics, Rehabilitation, and Applied Neurosciences, Hauppauge, NY, USA

⁴ Facultad Manuel Fajardo, Institute for Neurology and Neurosurgery, Universidad de Ciencias Médicas de la Habana, Habana, Cuba

⁵ Nazareth Academic Institute, Nazareth, Israel

Edited by:

Ahmed A. Moustafa, University of Western Sydney, Australia

Reviewed by:

Calixto Machado, Institute of Neurology and Neurosurgery, Cuba
Jorge L. Morales-Cuevas, Laboratory of Neuromodulation, USA

*Correspondence:

Gerry Leisman, The National Institute for Brain and Rehabilitation Sciences, ORT-Braude College of Engineering, 51 Snunit, PO Box 78, Karmiel 21982, Israel
e-mail: gerry.leisman@staff.nazareth.ac.il

Neural circuits linking activity in anatomically segregated populations of neurons in subcortical structures and the neocortex throughout the human brain regulate complex behaviors such as walking, talking, language comprehension, and other cognitive functions associated with frontal lobes. The basal ganglia, which regulate motor control, are also crucial elements in the circuits that confer human reasoning and adaptive function. The basal ganglia are key elements in the control of reward-based learning, sequencing, discrete elements that constitute a complete motor act, and cognitive function. Imaging studies of intact human subjects and electrophysiologic and tracer studies of the brains and behavior of other species confirm these findings. We know that the relation between the basal ganglia and the cerebral cortical region allows for connections organized into discrete circuits. Rather than serving as a means for widespread cortical areas to gain access to the motor system, these loops reciprocally interconnect a large and diverse set of cerebral cortical areas with the basal ganglia. Neuronal activity within the basal ganglia associated with motor areas of the cerebral cortex is highly correlated with parameters of movement. Neuronal activity within the basal ganglia and cerebellar loops associated with the prefrontal cortex is related to the aspects of cognitive function. Thus, individual loops appear to be involved in distinct behavioral functions. Damage to the basal ganglia of circuits with motor areas of the cortex leads to motor symptoms, whereas damage to the subcortical components of circuits with non-motor areas of the cortex causes higher-order deficits. In this report, we review some of the anatomic, physiologic, and behavioral findings that have contributed to a reappraisal of function concerning the basal ganglia and cerebellar loops with the cerebral cortex and apply it in clinical applications to attention deficit/hyperactivity disorder (ADHD) with biomechanics and a discussion of retention of primitive reflexes being highly associated with the condition.



Right Hemisphere Dysfunction in Subjects With Attention-Deficit Disorder With and Without Hyperactivity

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DOI: 10.1177/0883267389701200207

The attention-deficit disorder, with and without hyperactivity, is associated with defective attention, response inhibition and, in attention-deficit disorder with hyperactivity, with motor restlessness. In adults, inattention, defective response inhibition, and impulsiveness are more commonly seen in right hemisphere lesions. In the present study, we investigate possible right hemisphere dysfunctions in attention-deficit disorder with hyperactivity and attention-deficit disorder without hyperactivity. The right hemisphere performance of 60 teenagers, 16 having attention-deficit disorder with hyperactivity, 9 having attention-deficit disorder without hyperactivity, and 35 controls, selected clinically (DSM-III) and experimentally (through Continuous Performance Test and Paced Auditory Addition Task), with normal IQ was assessed using a wide-ranging battery of visuospatial, visuoperceptive, and visuoconstructive functions (Benton's Line Orientation, Benton's Visual Retention, Raven's Progressive Matrices, Wechsler Adult Intelligence Scale [WAIS] Block-Design, Rey's Complex Figure). Teenagers with attention-deficit disorder with and without hyperactivity performed significantly worse than controls. Greater differences were found between subjects with attention-deficit disorder without hyperactivity and control than between subjects with attention-deficit disorder with hyperactivity and control subjects. Our results seem to be consistent with right-hemisphere dysfunction, especially in subjects with attention-deficit disorder without hyperactivity. Additionally, WAIS Block-Design and Benton's Line Orientation are the visuospatial tests with the highest discriminant power to differentiate between controls, subjects with attention-deficit disorder without hyperactivity, and subjects with attention-deficit disorder with hyperactivity. (*J Child Neurol* 1997;12:107-115).

Attention Deficit/Hyperactivity Disorder as a Right Hemisphere Syndrome

Selective Literature Review and Detailed
Neuropsychological Case Studies

GERRY A. STEFANATOS *a*

AND JEANETTE WASSERSTEIN *ba*

*Cognitive Neurophysiology Laboratory, MossRehab Research Institute,
Albert Einstein Medical Center, Philadelphia, Pennsylvania 19141, USA*

A BSTRACT

: Recent studies of ADHD implicate well-defined neuroanatomical networks and neurochemical pathways in its pathophysiological basis. Considerable attention has focused on the role of anterior and superior frontal regions and portions of the basal ganglia, including the caudate nucleus and globus pallidus. This paper reviews a growing literature suggesting differential involvement of right hemisphere mechanisms specialized for behavioral regulation and attention. Supportive data are drawn from neuropsychology, neuroanatomy, and neurochemistry. In addition, three cases are presented that illustrate the complex role of right hemisphere dysfunction in adult manifestations of ADHD. We suggest that the pleomorphic presentations of ADHD can be understood in terms of a spectrum of disturbances in overlapping neural regions, especially involving frontal and parietal areas of the right hemisphere and their connections to subcortical structures (including the striatum, limbic

Martin H. Teicher, M.D., Ph.D.
*Director, Developmental Biopsychiatry
Research Program
Chief, Laboratory of Developmental
Psychopharmacology
McLean Hospital
115 Mill Street
Belmont, MA 02478-9106*



Harvard Medical School
Department of Psychiatry
Associate Professor
Phone: 617-855-2970
Fax: 617-855-3712
Email:
martin_teicher@hms.harvard.edu

Assessing the Influence of 'Brain Balancing' Exercises on Symptoms and Neurobiology in Children with Attention-Deficit Hyperactivity Disorder

A research protocol submitted by
Martin H. Teicher, M.D., Ph.D.
March 14, 2013

Attention-deficit hyperactivity disorder (ADHD) is one of the most common neuropsychiatric disorders of childhood, and it often persists into adulthood³. ADHD is characterized by a triad of symptoms: inattention, hyperactivity and impulsivity³. Although common, it is a serious disorder associated with a 10-fold increased incidence of antisocial personality disorder^{9,26}, up to 5-fold increased risk of drug abuse^{7,9}, 25-fold excess risk for institutionalization for delinquency¹⁶, and up to 9-fold increased risk of incarceration¹⁰. ADHD is often highly responsive to pharmacotherapy, but the gains are transient and wear off after each dose²³. To compound matters, compliance is usually poor¹⁴. Several attempts have been made to identify treatments that provide enduring benefits. EEG biofeedback has probably received the most interest as a potential treatment and the American Psychological Association currently rates neurofeedback as "Probably Efficacious," but in need of further study. An interesting approach that is practiced in the community, but has not been sufficiently evaluated involves exercises that supposedly foster right hemisphere development and right-left hemispheric integration. The focus on right-hemisphere development and right-left hemispheric integration fits with what we and others have observed neurobiologically^{4-6,15,25,27,28}. Hence, we are interested in assessing whether this type of treatment is associated with improvement in objective indices of symptom severity and in changes in resting T2-relaxation time and functional connectivity in corticostriatal-cerebellar regions of interest.

Assessing the Influence of 'Brain Balancing' Exercises on Symptoms and Neurobiology in Children with Attention-Deficit Hyperactivity Disorder

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Epigenetic mechanisms and environmental shaping of the brain during sensitive periods of development

Tania L. Roth^{1,2} and J. David Sweatt^{1,*}

¹ Department of Neurobiology and Evelyn F. McKnight Brain Institute, University of Alabama at Birmingham, Birmingham, AL 35294

Abstract

Experiences during early development profoundly affect development of the CNS to impart either risk for or resilience to later psychopathology. Work in the developmental neuroscience field is providing compelling data that epigenetic marking of the genome may underlie aspects of this process. Experiments in rodents continue to show that experiences during sensitive periods of development influence DNA methylation patterns of several genes. These experience-induced DNA methylation patterns represent stable epigenetic modifications that alter gene transcription throughout the lifespan and promote specific behavioral outcomes. We discuss the relevance of these findings to humans, and also briefly discuss these findings in the broader contexts of cognition and psychiatric disorder. We conclude by discussing the implications of these observations for future research.

DNA methylation changes that alter excitability may be involved in neuropsychiatric diseases

- Published on August 24, 2016 at 6:22 AM
- Diseases such as epilepsy, neuropathic pain, anxiety, depression, drug addiction and Alzheimer's are all associated with changes in the excitability of brain neurons. University of Alabama at Birmingham researchers show, for the first time, that the well-known mechanism of gene expression control -- dynamic changes in DNA methylation -- is also involved in changes to the excitability of neural cells.
- This suggests that DNA methylation changes that alter excitability may be a mechanism involved in neuropsychiatric disorders, and that the sites of such changes may offer a potential therapeutic target. The study was published today in *Science Signaling*.
- Changes in DNA methylation in brain cells has been an extremely active research area since these epigenetic changes were shown to alter the expression of genes needed to form and maintain long-term memories. Until now, a mechanistic understanding of how DNA methylation might influence the intrinsic membrane excitability of neurons, or IME, was lacking.

New insights into how the mind influences the body

- August 15, 2016
- Neuroscientists at the University of Pittsburgh have identified the neural networks that connect the cerebral cortex to the adrenal medulla, which is responsible for the body's rapid response in stressful situations. These findings, reported in the online Early Edition of the journal *Proceedings of the National Academy of Sciences* (PNAS), provide evidence for the neural basis of a mind-body connection.
- Specifically, the findings shed new light on how stress, depression and other mental states can alter organ function, and show that there is a real anatomical basis for psychosomatic illness. The research also provides a concrete neural substrate that may help explain why meditation and certain exercises such as yoga and Pilates can be so helpful in modulating the body's responses to physical, mental and emotional stress.
- "Our results turned out to be much more complex and interesting than we imagined before we began this study," said senior author Peter L. Strick, Ph.D., Thomas Detre Chair of the Department of Neurobiology and scientific director of the University of Pittsburgh Brain Institute.
- In their experiments, the scientists traced the neural circuitry that links areas of the [cerebral cortex to the adrenal medulla \(the inner part of the adrenal gland, which is located above each kidney\)](#). [The scientific team included lead author Richard P. Dum, Ph.D., research associate professor in the Department of Neurobiology; David J. Levinthal, M.D., Ph.D., assistant professor in the Department of Medicine; and Dr. Strick.](#)
- The scientists were surprised by the sheer number of [neural networks they uncovered](#).
- Another surprising result was that motor areas in the cerebral cortex, involved in the planning and performance of movement, provide a substantial input to the adrenal medulla. One of these areas is a portion of the [primary motor cortex that is concerned with the control of axial body movement and posture](#). [This input to the adrenal medulla may explain why core body exercises are so helpful in modulating responses to stress. Calming practices such as Pilates, yoga, tai chi and even dancing in a small space all require proper skeletal alignment, coordination and flexibility.](#)

Early-life infections may be risk factor for developmental disorders later in life

- Published on August 19, 2016 at 3:11 AM
- Zika is the example we all know about right now," said neuroscientist Jaclyn Schwarz, assistant professor in the University of Delaware's Department of Psychological and Brain Sciences. "But any infection in a pregnant woman can affect the fetus, and we also know that any immune response [the body's defense against infection] does affect your brain."
- Schwarz recently was awarded a five-year, \$1.8 million grant from the National Institutes of Health to support her research on infections that occur either before or shortly after birth.
- She's looking into whether such an infection -- from bacteria or any other source that activates the body's immune response to counteract it -- can be a risk factor for developmental disorders years later.
- Among the possible disorders are learning disabilities and autism, generally diagnosed in early childhood, and schizophrenia, often diagnosed in late adolescence.
- "We know from previous research that if Mom has influenza in the second or third trimester, there's an increased risk of mental health problems later in the child's life," Schwarz said.

The Early Development of the Autonomic Nervous System Provides a Neural Platform for Social Behaviour: A Polyvagal Perspective

Stephen W. Porges[✉] and Senta A. Furman

Brain-Body Center, Department of Psychiatry, University of Illinois at Chicago, Chicago, IL, USA

We present a biobehavioural model that explains the neurobiological mechanisms through which measures of vagal regulation of the heart (e.g. respiratory sinus arrhythmia) are related to infant self-regulatory and social engagement skills. The model describes the sequential development of the neural structures that provide a newborn infant with the ability to regulate physiological state in response to a dynamically changing postpartum environment. Initially, the newborn uses primitive brainstem-visceral circuits via ingestive behaviours as the primary mechanism to regulate physiological state. However, as cortical regulation of the brainstem improves during the first year of life, reciprocal social behaviour displaces feeding as the primary regulator of physiological state. The model emphasizes two sequential phases in neurophysiological development as the fetus transitions to postpartum biological and social challenges: (1) the development of the myelinated vagal system during the last trimester and (2) the development of cortical regulation of the brainstem areas regulating the vagus during the first year postpartum.

The Early Development of the Autonomic Nervous System Provides a Neural Platform for Social Behaviour: A Polyvagal Perspective

Developmentally, as skills of state regulation improve, the central nervous system expands to promote enhanced cognition and greater control over peripheral motor systems. These global systems (autonomic, cognitive, and motor) mature in combination and enable the maturing infant to become more independent and explorative in a complex environment.

The Early Development of the Autonomic Nervous System Provides a Neural Platform for Social Behaviour: A Polyvagal Perspective

To accommodate both fight-flight and social engagement behaviours, the new mammalian vagus evolved to enable rapid, adaptive shifts in autonomic state. The mammalian myelinated vagus functions as an active vagal brake (Porges, Doussard- Roosevelt, Portales, & Greenspan, 1996) in which inhibition and recovery of the vagal tone to the heart can rapidly mobilize or calm an individual. Tonic vagal influences to the sinoatrial node (i.e. the primary cardiac pacemaker) produce a resting heart rate that is substantially lower than the intrinsic rate of the pacemaker alone. When vagal tone, through myelinated vagal pathways, to the pacemaker is high, the vagus acts as a restraint, or brake, limiting the rate at which the heart can beat and functionally calming the individual. When vagal tone to the pacemaker is low, there is little or no inhibition of the pacemaker, and the heart rate increases. The vagal brake construct may be used to describe functional modulation of heart rate by myelinated vagal efferent pathways.

The Early Development of the Autonomic Nervous System Provides a Neural Platform for Social Behaviour: A Polyvagal Perspective

We propose that the developmental changes in the neural pathways that regulate autonomic state provide a neural platform to support the expanding abilities of the infant to engage objects and people in a dynamically changing environment. Thus, the emerging behavioural repertoire and social-interactive needs of the rapidly developing young infant should be studied within the context of the maturational changes in the autonomic nervous system.

The Ingestive response

Since the structures involved in sucking, swallowing, vocalizing, and breathing are all linked to the myelinated vagus, the functioning of these behaviors and RSA, may provide an early indicator of the functional status of a system that will later be involved in social engagement behaviors.

Studies have shown that in response to sucrose, reduction in RSA and corresponding increase in heart rate paralleled increase sucking frequency. After the heart rate returned to presucrose levels.

These findings illustrate that in a healthy neonate there is a coordinated ingestive response in which the vagal brake is systematically removed to support the increase metabolic demand of sucking, this return to baseline was not seen in premature infants born before 30 weeks of gestation.



The Ingestive –Vagal Reflex

Older preterm infants modulate the vagal brake during feeding. This ingestive –vagal reflex might be mediated solely at the brainstem level and might not be sensitive to increasing number and efficiency of corticobulbar pathways connecting the cortex with the source nucleus of the myelinated vagus, the Nucleus Ambiguus, which arise during maturation.

From an evolutionary perspective, the adaptive consequence of these higher order neuroanatomical changes would enable the older infant to use social cues to regulate the vagal brake.

The loving caregivers facial features and vocal prosody trigger temporal corticolimbic pathways that dampen defensive reactions and recruit the vagal brake to calm.

In contrast vocal features of a stranger might inhibit the vagal brake to allow mobilizing, protesting and defensive behavior

If there is some alteration, delay or diminished ability to process any of this information in the developing infant, then they might not be able to develop this distinction and then every voice may seem like a stranger and they may always have the Vagal Brake inhibited



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Original article

Reduced cardiac parasympathetic activity in children with autism

Xue Ming^{a,b,*}, Peter O.O. Julu^c, Michael Brimacombe^d, Susan Connor^e, Mary L. Daniels^d

^aDepartment of Neuroscience, New Jersey Medical School, UMDNJ, Newark, 90 Bergen Street, DOC 8100, NJ 07103, USA

^bCenter for Childhood Exposure and Assessment, Robert Wood Johnson Medical School, UMDNJ, Piscataway, NJ 08854, USA

^cDepartment of Neurology, Peripheral Nerve and Autonomic Unit, Central Middlesex Hospital, Park Royal, London, UK

^dDepartment of Preventive Medicine, School of Public Health, UMDNJ, Newark, NJ 07103, USA

^eDepartment of Neurology and Developmental Medicine, Kennedy Krieger Institute, Baltimore, MD 21205, USA

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Abstract

Many of the clinical symptoms of autism suggest autonomic dysfunction. The aim of this study was to measure baseline cardiovascular autonomic function in children with autism using the NeuroScope, a device that can measure this brainstem function in real time. Resting cardiac vagal tone (CVT), cardiac sensitivity to baroreflex (CSB), mean arterial blood pressure (MAP), diastolic blood pressure (DBP), systolic blood pressure (SBP) and heart rate (HR) were recorded in three different groups of children. The symptomatic group ($n=15$) consisted of those with autism who exhibited symptoms or signs of autonomic dysfunction. The asymptomatic group ($n=13$) consisted of children with autism but without symptoms or signs of autonomic dysfunction and the healthy children were in the control group ($n=17$). The CVT and CSB were significantly lower in association with a significant elevation in HR, MAP and DBP in all children with autism compared with the healthy controls. Further more, the levels of CVT and CSB were lower in the symptomatic than in the asymptomatic group. The levels of CVT and CSB were not related to age in all the three groups. These results suggest that there is low baseline cardiac parasympathetic activity with evidence of elevated sympathetic tone in children with autism whether or not they have symptoms or signs of autonomic abnormalities.

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Keywords: Autism; Brainstem; Parasympathetic nerves; Sympathetic nerves; NeuroScope



The Development of The ANS

The development of the autonomic nervous system in the human fetus mirrors the broader phylogenetic progression already described. The phylogenetically oldest vertebrate autonomic system, which relies on unmyelinated efferent vagal fibers originating from the Dorsal Motor Nucleus of the Vagus, is also embryologically the earliest system to develop in utero. An immature, undifferentiated DMNX first appears in the brainstem at 9 weeks gestation (Cheng, Zhou, Qu, Ashwell, & Paxinos, 2004; Nara, Goto, & Hamano, 1991).

Magnocellular subdivisions become visible by 13 weeks, and clear demarcation of DMNX subnuclei, including the lateral cardiomotor subnucleus, occurs by 23 weeks. At 28 weeks, all magnocellular subnuclei are considered essentially mature. Some however, including Nara et al (1991), believe that there must be some postnatal changes that are not considered to have much functional significance or physiological consequence in the neonate.

The Development of The ANS

The other major component of the parasympathetic, cardioinhibitory ANS is the newest myelinated vagal system, which originates in the Nucleus Ambiguus, this system as predicted by the polyvagal theory, develops last in the fetus and continues to functionally develop well into the first postnatal year. Mature neurons appear in the rostral NA by 8 or 9 weeks gestation and fill the nucleus by 12.5 weeks (Brown, 1990). Unlike mature neurons in the lateral subnucleus of the DMNX, however, axons of these mature neurons have not yet reached cardiac tissue to exert cardioinhibitory effects. Myelination of the NA does not begin until 23 weeks gestation and increases linearly from 24 - 40 weeks gestation and continues during the first year.

The Development of The ANS

Development of the sympathetic, cardioexcitatory, ANS is less well described in the literature. Phylogenetically this large catecholaminergic system appears before the mammalian NA system and after the older DMNX Vagus. This system should begin developing in the human fetus sometime between the two parasympathetic systems.

Postganglionic cardiomotor nuclei lie mostly within the cardiothoracic and middle cervical ganglion, which lie caudal to the sympathetic superior cervical ganglion. Unlike the two vagal circuits which exert mostly chronotropic (slowing heart), sympathetic activity leads to both chronotropic (increasing heart rate) by innervating pacemaker tissue and ionotropic (increasing cardiac contractility) by innervating ventricular myocardium. Using 24-hour fetal heart rate monitoring in 28 healthy women, Kinatra, Zarnadze, and Kashakashvili (2005) reported that fetal locomotor activity increases between 16 and 20 weeks gestation. At this stage increases in activity are accompanied by corresponding increases in heart rate, which returns to normal during quiet fetal periods. Since the NA is not functioning yet the increase in heart rate must be due to activation of the sympathetic system.

Furthermore researchers have interpreted an absence of such a coordinated heart rate increase with increased locomotion by 24 weeks gestation as "developmental retardation"

The 10 Hz Frequency: A Fulcrum For Transitional Brain States

E. Garcia-Rill^{1,*}, S. D'Onofrio¹, B. Luster¹, S. Mahaffey¹, F. J. Urbano², and C. Phillips^{1,3}

E. Garcia-Rill: GarciaRillEdgar@uams.edu; S. D'Onofrio: SNDonofrio@uams.edu; B. Luster: BRLuster@uams.edu; S. Mahaffey: SMahaffey@uams.edu; F. J. Urbano: fjurbano@fbmc.fcen.uba.ar; C. Phillips: cphillips@astate.edu

¹Center for Translational Neuroscience, University of Arkansas for Medical Sciences, Little Rock, AR, 72205, US

²IFIBYNE-CONICET, University of Buenos Aires, Argentina

³Department of Physical Therapy, Arkansas State University, Jonesboro, AR, 72401

Abstract

A 10 Hz rhythm is present in the occipital cortex when the eyes are closed (alpha waves), in the precentral cortex at rest (*mu* rhythm), in the superior and middle temporal lobe (*tau* rhythm), in the inferior olive (projection to cerebellar cortex), and in physiological tremor (underlying all voluntary movement). These are all considered resting rhythms in the waking brain which are "replaced" by higher frequency activity with sensorimotor stimulation. That is, the 10 Hz frequency fulcrum is replaced on the one hand by lower frequencies during sleep, or on the other hand by higher frequencies during volition and cognition. The 10 Hz frequency fulcrum is proposed as the natural frequency of the brain during quiet waking, but is replaced by higher frequencies capable of permitting more complex functions, or by lower frequencies during sleep and inactivity. At the center of the transition shifts to and from the resting rhythm is the reticular activating system, a phylogenetically preserved area of the brain essential for preconscious awareness.



The Cerebellum, Sensitive Periods, and Autism

Samuel S.-H. Wang,^{1,*} Alexander D. Kloth,¹ and Aleksandra Badura¹

¹Princeton Neuroscience Institute and Department of Molecular Biology, Princeton University, Princeton, NJ 08544, USA

*Correspondence: sswang@princeton.edu

<http://dx.doi.org/10.1016/j.neuron.2014.07.016>

Cerebellar research has focused principally on adult motor function. However, the cerebellum also maintains abundant connections with nonmotor brain regions throughout postnatal life. Here we review evidence that the cerebellum may guide the maturation of remote nonmotor neural circuitry and influence cognitive development, with a focus on its relationship with autism. Specific cerebellar zones influence neocortical substrates for social interaction, and we propose that sensitive-period disruption of such internal brain communication can account for autism's key features.

Vestibular –Related Impairments in Children

Tsuzuku and Kaga and others reported learning disabilities and delayed development of walking and balance abilities in children with peripheral vestibular hypofunction as measured with caloric and/or rotary chair tests. Rine et al reported that children with SNHL and vestibular hypofunction .. Presented with delayed maturation of vestibular and vision ratios on posturography testing. These children had a progressive delay in gross motor development.

Children with abnormal vestibular function tests develop head control and independent walking significantly later than typically developing children.

These findings concur with report by Weiner-vacher ,who reported acquisition of walking ability was related to measures of otolith ,not canal, vestibular function

Lateral asymmetries in infancy: implications for the development of the hemispheres.

- Neurosci Biobehav Rev. 1996 Winter;20(4):571-86.
- [Trevarthen C.](#)
- Department of Psychology, University of Edinburgh, UK.
- **Abstract**
- Cerebral asymmetry of cognitive processing of stimulus information is commonly viewed as a neocortical phenomenon. However, a number of lines of evidence give innate asymmetry of brainstem motivating systems, which anticipate experience, a key role. Spontaneous asymmetries of gesture and emotion can be observed in infants, who entirely lack language and visuo-constructive skills. Motives for communication in early life may direct subsequent development of complementary cognitive systems in left and right hemispheres. In split-brain monkeys, lateralized motive sets, intentions for manipulation by one hand, can determine which hemisphere will see and learn. Evolutionary antecedents of cerebral asymmetry appear to affect motivation, social signalling and bimanual coordination, with secondary effect in perceptual processing and learning. The hemispheres of adult humans differ in links with neurochemical system that regulate motor initiatives, exploration and attention, and the approach/withdrawal balance in social encounters. Asymmetries in emotional and communicative behaviour in infancy support evidence that an Intrinsic Motive Formation emerging in the embryo human brain stem regulates asymmetries in development and in functioning of the cerebral cortex.

Dr. Stephen Porges' Research May Support Berard's and Tomatis' Theory on Middle Ear Muscle Dysfunction

- **Dr. Stephen Porges' Research May Support Berard's and Tomatis' Theory on Middle Ear Muscle Dysfunction**
- Stephen Porges, Ph.D., a professor of Human Development at the University of Maryland, may be closing in on the reason why auditory integration training (AIT) and other similar auditory interventions may be beneficial to children with autism and other related disorders. Dr. Porges' work has been described in a previous issue of *The Sound Connection*, but we are learning more about his hypotheses and research findings (see *The Sound Connection*, Vol. 6, No. 4).
- Similar to the works of Drs. Alfred Tomatis and Guy Berard, Dr. Porges' research has focused on the two muscles in the middle ear--the tensor tympani and the stapedius. Porges has found that the same nerves that control these two muscles also control vocalization, facial expression, heart rate and breathing.

-Not for Public Dissemination-

The Basal Ganglia: Motor and Cognitive Relationships in a Clinical Neurobehavioral Context

Gerry Leisman^{1,2,3} Robert Melillo^{1,2,3}

¹F.R. Carrick Institute for Clinical Ergonomics, Rehabilitation, and Applied Neurosciences Garden City
New York USA

²The National Institute for Brain and Rehabilitation Sciences, Nazareth, Israel

³Nazareth Academic Institute, Nazareth, Israel

ABSTRACT

New information about basal ganglia and cerebellar connections with the cerebral cortex has prompted a reevaluation of the role of the basal ganglia in cognition. We know that the relation between the basal ganglia and the cerebral cortical region allow for connections organized into discrete circuits. Rather than serving as a means for widespread cortical areas to gain access to the motor system, these loops reciprocally interconnect a large and diverse set of cerebral cortical areas with the basal ganglia. The properties of neurons within the basal ganglia or cerebellar components of these circuits resemble the properties of neurons within the cortical areas subserved by these loops. For example, neuronal activity within basal ganglia and cerebellar loops with motor areas of the cerebral cortex is highly correlated with parameters of movement, while neuronal activity within basal ganglia and cerebellar loops with areas of the prefrontal cortex is more related to aspects of cognitive function. Thus, individual loops appear to be involved in distinct behavioral functions. Studies of basal ganglia and cerebellar pathology support this conclusion. Damage to the basal ganglia or cerebellar components of circuits with motor areas of cortex leads to motor symptoms, whereas damage of the subcortical components of circuits with non-motor areas of cortex causes higher-order deficits. In this report, we review some of the new anatomical, physiological and behavioral findings that have contributed to a reappraisal of function concerning the basal ganglia and cerebellar loops with the cerebral cortex and apply it in clinical applications to obsessive-compulsive disorder, Tourette's, and attention-deficit hyperactivity disorder as examples of how compromise at different points in the system may yield similar but different clinical results..

Key Words: Basal ganglia, cognition, frontal lobes, direct pathways, indirect pathways, OCD, Tourette's,

The Basal Ganglia: Motor and Cognitive Relationships in a Clinical Neurobehavioral Context

The Basal Ganglia in the Context of Behavior

Gerry Leisman^{1,2,3,4} Robert Melillo^{1,2,3} Frederick R. Carrick^{1,5}

¹F.R. Carrick Institute for Clinical Ergonomics, Rehabilitation, and Applied Neurosciences Garden City New York USA

²The National Institute for Brain and Rehabilitation Sciences, Nazareth, Israel

³Nazareth Academic Institute, Nazareth, Israel

⁴Biomedical Engineering, Dept. Biomechanics, ORT-Braude College of Engineering, Carmiel, Israel

⁵Carrick Institute for Graduate Studies, Cape Canaveral, Florida USA

ABSTRACT

New information about basal ganglia and cerebellar connections with the cerebral cortex has prompted a reevaluation of the role of the basal ganglia in cognition. We know that the relation between the basal ganglia and the cerebral cortical region allow for connections organized into discrete circuits. Rather than serving as a means for widespread cortical areas to gain access to the motor system, these loops reciprocally interconnect a large and diverse set of cerebral cortical areas with the basal ganglia. The properties of neurons within the basal ganglia or cerebellar components of these circuits resemble the properties of neurons within the cortical areas subserved by these loops. For example, neuronal activity within basal ganglia and cerebellar loops with motor areas of the cerebral cortex is highly correlated with parameters of movement, while neuronal activity within basal ganglia and cerebellar loops with areas of the prefrontal cortex is more related to aspects of cognitive function. Thus, individual loops appear to be involved in distinct behavioral functions. Studies of basal ganglia and cerebellar pathology support this conclusion. Damage to the basal ganglia or cerebellar components of circuits with motor areas of cortex leads to motor symptoms, whereas damage of the subcortical components of circuits with non-motor areas of cortex causes higher-order deficits. In this report, we review some of the new anatomical, physiological and behavioral findings that have contributed to a reappraisal of function concerning the basal ganglia and cerebellar loops with the cerebral cortex and apply it in clinical applications to obsessive-compulsive disorder, Tourette's, and attention-deficit hyperactivity disorder as examples of how compromise at different points in the system may yield similar but different clinical results..

Synaptic Shortcut

Newly discovered brain pathway overturns anatomy, could solve antipsychotic mystery

• By STEPHANIE DUTCHEN

• March 6, 2015

- It's been "known" for decades: Sensory, motor and cognitive signals come in from the brain's cortex and are processed in the basal ganglia. The basal ganglia then send out signals that get routed through the thalamus and back to the cortex.
- Except not always, according to a new study in animal models. The basal ganglia can also talk back directly to the cortex, no thalamus required.
- The findings, published this week in *Nature*, [upend classic anatomy and provide possible new insights into psychiatric diseases such as schizophrenia.](#)
- "Our results redefine the architecture of the basal ganglia and the mechanisms for subcortical-cortical feedback, which are absolutely crucial for coordinated motor behavior and reward learning
- Researchers believe the basal ganglia help organisms decide how to move and behave at a given moment, including control of voluntary movement, procedural and reward learning, and habit forming and breaking.
- Many disorders of motion or behavior have their roots in this area of the brain, ranging from obsessive-compulsive disorder to Parkinson's disease.
- "The role these subcortical regions play in many neurological and psychiatric diseases is continuing to be appreciated," said Saunders. "It's really important to better understand how they're organized."

Attention Deficit/Hyperactivity Disorder as a Right Hemisphere Syndrome Selective Literature Review and Detailed Neuropsychological Case Studies

• GERRY A. STEFANATOS ^a
• AND JEANETTE WASSERSTEIN ^{ba}
• *Cognitive Neurophysiology Laboratory, MossRehab Research Institute,*

• A BSTRACT

• : Recent studies of ADHD implicate well-defined neuroanatomical networks and neurochemical pathways in its pathophysiological basis. Considerable attention has focused on the role of anterior and superior frontal regions and portions of the basal ganglia, including the caudate nucleus and globus pallidus. This paper reviews a growing literature suggesting differential involvement of right hemisphere mechanisms specialized for behavioral regulation and attention. Supportive data are drawn from neuropsychology, neuroanatomy, and neurochemistry. In addition, three cases are presented that illustrate the complex role of right hemisphere dysfunction in adult manifestations of ADHD. We suggest that the pleomorphic presentations of ADHD can be understood in terms of a spectrum of disturbances in overlapping neural regions, especially involving frontal and parietal areas of the right hemisphere and their connections to subcortical structures (including the striatum, limbic

Olfactory impairments in child attention-deficit/hyperactivity disorder.

- Karsz FR, Vance A, Anderson VA, Brann PG, Wood SJ, Pantelis C, Brewer WJ. J Clin Psychiatry. 2008 Sep;69(9):1462-1468.
- **OBJECTIVE:** This study compared unilateral olfactory identification abilities in children with and without attention-deficit/hyperactivity disorder (ADHD) and evaluated the utility of the University of Pennsylvania Smell Identification Test (UPSIT) as a potential screening tool for the diagnosis of ADHD.
- **RESULTS:** Children with ADHD demonstrated significantly poorer olfactory identification ability compared to healthy controls ($p < .01$). A significant right nostril advantage for smell identification was evident in the control group ($p < .01$), whereas significant right nostril impairment was evident among the children with ADHD ($p < .01$).
- **CONCLUSION:** The results provide the first evidence of olfactory identification deficits in children with ADHD. As such deficits implicate orbitofrontal regions, this finding is consistent with previous reports of prefrontal compromise in children with ADHD.

EEG COHERENCE MEASURES FUNCTIONAL DISCONNECTIVITIES IN AUTISM

G. Leisman¹, R. Melillo^{2, 1} *Acta Paediatrica*, 2009, 98:460, 28-29.

F. R. Carrick Research Institute, Leeds Metropolitan Univ. UK & Univ. of Haifa, Haifa, Israel, ²F. R. Carrick Research Institute, Ronkonkoma, NY, USA

Background: Theoretical conceptions of autistic spectrum disorder (ASD) suggest abnormalities in connections among distributed neural systems. EEG coherence studies had a twofold objective: to scrutinize the theory of cortical optimization in autism and detect coherence between cortical areas in specific frequency bands in autistics and controls.

Methods: Functional connectivity was assessed with coherence between electrode pairs in narrow frequency bands among 18 adult ASDs and 18 controls in an eyes-closed resting state.

Results: Explorative analysis in 6 frequency bands (0.5-31.5 Hz) indicated locally elevated coherence in autistics compared to a more distributed coherence. Autistics demonstrated elevated local coherence, especially in the left hemisphere, frontal, and temporal regions in the 3-6 Hz frequency range. In the 8-10 Hz, globally reduced coherence was evident for ASDs within frontal regions and between frontal and all other scalp regions. Coherence brain maps revealed more pronounced and widespread increases in coherences in the 8-10 Hz band in the low optimized ASD individuals than in the more highly optimized controls and corroborated for both groups by multivariate permutation tests. These tests revealed additional differences between the low- and the high-proficiency group also for coherences within the 13-18 Hz and the 18.5-31.5 Hz bands. ASDs exhibited significantly greater relative power between 3 and 6 Hz.

Conclusions: Robust patterns of over- and under-connectivity were apparent at distinct spatial and temporal scales in ASDs in the eyes-closed resting state. Autistics demonstrate underactivity of right hemisphere and overactivity of left relative to controls.



Functional connectivity in a baseline resting-state network in autism

In, Press, *NeuroReport* RESTING STATE NETWORK IN AUTISM

Vladimir L. Cherkassky

Rajesh K. Kana

Timothy A. Keller

Marcel Adam Just

Carnegie Mellon University

Center for Cognitive Brain Imaging,

Department of Psychology,

Pittsburgh, PA 15213

Abstract: Brain activity in people with high-functioning autism has been shown to be atypical in a number of ways, including reduced synchronization across areas of fMRI-measured activation. This activation atypicality has been observed mostly during the performance of cognitive tasks. This study compares the resting-state network of 57 participants with autism and 57 control participants matched for age and IQ. The results indicate that both groups have a resting-state network which is very similar both in volume and in organization, but in autism, this network is much more loosely connected. This functional underconnectivity was observed in the anteriorposterior connections. The results expand the theory of cortical underconnectivity in autism to the resting state of the brain.

An Exploration of Right-Hemisphere Contributions to the Pragmatic Impairments of Autism

Authors: Ozonoff S.; Miller J.N.

Source: [Brain and Language](#), Volume 052, Number 3, 1996, pp. 411-434(24)

Abstract:

This study examined the potential contribution of the right hemisphere to the communicative impairments of autism. Pragmatic language measures sensitive to right-hemisphere damage were administered to nonretarded adults with autism and to controls matched on age and intellectual ability. The experimental battery included measures of humor, inference, and indirect request comprehension. Autistic subjects performed significantly less well than controls on all measures, replicating results of an earlier investigation by Rumsey and Hanahan (Journal of Clinical and Experimental Neuropsychology, 12, 81, 1990). The performance of the autistic group on the three tasks was also similar to that of right-hemisphere stroke patients reported previously (Molloy, Brownell, & Gardner, in Y. Joanette and H. M. Brownell (Eds.), Discourse ability and brain damage: Theoretical and empirical perspectives, New York: Springer-Verlag, 1990, pp. 113-130). Generalizability of these results and implications for the neuropathology of autism are discussed.

Autistic Spectrum Disorders as Functional Disconnection Syndrome

Reviews in Neurosciences 2009

Robert Melillo¹ and Gerry Leisman^{1,2}

¹F. R. Carrick Institute for Clinical Ergonomics, Rehabilitation, and Applied Neuroscience of Leeds Metropolitan University, Leeds, UK

¹, ²Department of Communication Disorders, University of Haifa, Mt. Carmel, Haifa, Israel 31905

Abstract

We outline in this paper the basis of how functional disconnection with reduced activity and coherence in the right hemisphere would explain all of the symptoms of autistic spectrum disorder as well as the observed increases in sympathetic activation. If the problem of autistic spectrum disorder is primarily one of desynchronization and ineffective interhemispheric communication, then the best way to address the symptoms is to improve coordination between areas of the brain. To do that the best approach would include multimodal therapeutics that would include a combination of somatosensory, cognitive, behavioral, and biochemical interventions all directed at improving overall health, reducing inflammation and increasing right hemisphere activity to the level that it becomes temporally coherent with the left hemisphere. We hypothesize that the unilateral increased hemispheric stimulation has the effect of increasing the temporal oscillations within the thalamocortical pathways bringing it closer to the oscillation rate of the adequately functioning hemisphere. We propose that increasing the baseline oscillation speed of one entire hemisphere will enhance the coordination and coherence between the two hemispheres allowing for enhanced motor and cognitive binding.

QEEG Spectral and Coherence Assessment of Autistic Children in Three Different Experimental Conditions.

- [J Autism Dev Disord. 2013 Sep 19. \[Epub ahead of print\]](#)
- [Machado C, Estévez M, Leisman G, Melillo R, Rodríguez R, Defina P, Hernández A, Pérez-Nellar J, Naranjo R, Chinchilla M, Garófalo N, Vargas J, Beltrán C.](#)

Source: Department of Clinical Neurophysiology, Institute of Neurology and Neurosurgery, 29 y D, Vedado, 10400, Havana, La Habana, Cuba, braind@infomed.sld.cu.

- Abstract

We studied autistics by quantitative EEG spectral and coherence analysis during three experimental conditions: basal, watching a cartoon with audio (V-A), and with muted audio band (VwA). Significant reductions were found for the absolute power spectral density (PSD) in the central region for delta and theta, and in the posterior region for sigma and beta bands, lateralized to the right hemisphere. When comparing VwA versus the V-A in the midline regions, we found significant decrements of absolute PSD for delta, theta and alpha, and increments for the beta and gamma bands. In autistics, VwA versus V-A tended to show lower coherence values in the right hemisphere. An impairment of visual and auditory sensory integration in autistics might explain our results.

ANATOMIC AND FUNCTIONAL CONNECTIVITY RELATIONSHIP IN AUTISTIC CHILDREN DURING THREE DIFFERENT EXPERIMENTAL CONDITIONS

Authors: Calixto Machado¹; Rafael Rodríguez²; Mario Estévez¹; Gerry Leisman^{3,4,5}; Robert Melillo⁶; Mauricio Chinchilla¹; Liana Portela¹

ABSTRACT

We studied 21 autistic children, to determine the relationship between the anatomic (AC) vs. functional (FC) connectivity, considering short-range and long-range brain networks. AC was assessed by the DW-MRI technique and FC by EEG coherence calculation, in three experimental conditions: basal, watching a popular cartoon with audio (V-A), and with muted audio track (VwA). For short-range connections, basal records, we found statistical significant correlations for all EEG bands in the left hemisphere, meanwhile in the right hemispheres no significant correlation for fast EEG frequency bands were found. For the V-A condition, significant correlations mainly diminished for the left hemisphere; for the right hemisphere again no significant correlations for the fast EEG frequency bands were found. For the VwA condition, significant correlations for the rapid EEG frequencies mainly disappeared for the right hemisphere. For long-range connections, basal records, similar correlations were found for both hemispheres. For the right hemisphere significant correlations incremented to all EEG bands for the V-A condition, but these significant correlations disappeared for the fast EEG frequencies in the VwA condition. It appears that in a resting-state condition, AC is better associated with functional connectivity for short-range connections in the left hemisphere. V-A experimental condition enriches AC and FC association for long-range connections in the right hemisphere. This might be related to an effective connectivity improvement due to full video stimulation (visual and auditory). An impaired audio-visual interaction in the right hemisphere might explain why significant correlations disappeared for the fast EEG frequencies in the VwA experimental condition.

Environmental Enrichment as an Effective Treatment for Autism: A Randomized Controlled Trial.

By Woo, Cynthia C.; Leon, Michael

Behavioral Neuroscience, May 20, 2013, No Pagination Specified.

Abstract

Enriched sensorimotor environments enable rodents to compensate for a wide range of neurological challenges, including those induced in animal models of autism. Given the sensorimotor deficits in most children with autism, we attempted to translate that approach to their treatment. In a randomized controlled trial, 3–12 year-old children with autism were assigned to either a sensorimotor enrichment group, which received daily olfactory/tactile stimulation along with exercises that stimulated other paired sensory modalities, or to a control group. We administered tests of cognitive performance and autism severity to both groups at the initiation of the study and after 6 months. Severity of autism, as assessed with the Childhood Autism Rating Scale, improved significantly in the enriched group compared to controls. Indeed, 42% of the enriched group and only 7% of the control group had what we considered to be a clinically significant improvement of 5 points on that scale. Sensorimotor enrichment also produced a clear improvement in cognition, as determined by their Leiter-R Visualization and Reasoning scores. At 6 months, the change in average scores for the enriched group was 11.3 points higher than that for the control group. Finally, 69% of parents in the enriched group and 31% of parents in the control group reported improvement in their child over the 6-month study. Environmental enrichment therefore appears to be effective in ameliorating some of the symptoms of autism in children. (PsycINFO Database Record (c) 2013 APA, all rights reserved)



Interhemispheric Asymmetry In EEG Photoc Driving Coherence In Childhood Autism

1. Clin Neurophysiol. 2009 Nov 30. [Epub ahead of print]

[Lazarevi VV](#), [Pontes A](#), [Mitrofanov AA](#), [Deazevedo LC](#). Laboratory of Neurobiology and Clinical Neurophysiology, Fernandes Figueira Institute, Oswaldo Cruz Foundation, Ministry of Health, Rio de Janeiro, Brazil.

OBJECTIVE: Examination of the EEG photic driving coherence during intermittent photic stimulation in autistic patients with relatively intact verbal and intellectual functions in order to enhance the likely latent interhemispheric asymmetry in neural connectivity. **METHODS:** Fourteen autistic boys, aged 6-14 years, free of drug treatment, with I.Q. 91.4+/-22.8, and 19 normally developing boys were subject to stimulation of 12 fixed frequencies of 3-27Hz. The number of high coherent connections (HCC) (magnitude squared coherence >0.6-0.8) was estimated among 7 leads in each hemisphere. **RESULTS:** In contrast to the spectral characteristics showing the right hemisphere deficit in the photic driving reactivity, the number of HCC differentiated the groups only in the left hemisphere where it was higher in autistics at the EEG frequencies corresponding to those of stimulation at 6-27Hz without asymmetry at other frequencies, the left-side prevalence increasing with frequency. No asymmetry was observed in the resting state.

CONCLUSIONS: Spectral and coherence characteristics of the EEG photic driving show different aspects of latent **abnormal interhemispheric asymmetry in autistics: the right hemisphere "hyporeactivity" and potential "hyperconnectivity" of likely compensatory nature in the left hemisphere.** **SIGNIFICANCE:** The EEG photic driving can reveal functional topographic alterations not present in the spontaneous EEG.

PMID: 19951847 [PubMed - as supplied by publisher]

Spectral Analysis of Heart Rate Variability

Mario Estévez¹, Calixto Machado¹, Gerry Leisman,^{2,3,4,5} Robert Melillo^{2,4}, Adrián Hernández-Cruz^{1,5}, Talía Estévez-Hernández⁶, Asdrúbal Arias-Morales¹, Andrés Machado⁷, and Julio Montes-Brown⁸.

¹National Institute of Neurology and Neurosurgery, MINSAP, Havana, Cuba, ²The National Institute for Brain and Rehabilitation Sciences, Nazareth, Israel, ³Department Mechanical Engineering, O.R.T.-Braude College of Engineering, Karmiel, Israel, ⁴F. R. Carrick Institute for Clinical Ergonomics, Rehabilitation, and Applied Neuroscience, ⁵University of Medical Sciences "Manuel Fajardo Rivero," Havana, Cuba, ⁶Pontifical Catholic University of Puerto Rico, Ponce, Puerto Rico, ⁷Faculty of Biology, Havana University, Havana, Cuba, ⁸University Hospital "Ernesto Guevara de la Serna", Las Tunas, Cuba.

Abstract

Spectral analysis (SA) has been extensively applied to the assessment of heart rate variability. Traditional methods require the transformation of the original non-uniformly spaced electrocardiogram RR interval series into regularly spaced ones, using interpolation or other approaches. The Lomb-Scargle (L-S) method uses the raw original RR series avoiding different artifacts introduced by traditional SA methods, but it has been scarcely used in clinical settings. RR series recorded from 120 healthy participants (17–25 years) of both genders, during a resting condition, using four SA methods, including the Classic modified periodogram, the Welch procedure, the autoregressive Burg method and the L-S one. The efficient implementation of the L-S algorithm, with the added possibility of application of a set of options for the RR series pre-processing, developed by (Eleuteri et al., 2012), and also the results obtained in this study, showed that the L-S method can be a good choice for future clinical studies. The L-S method seems particularly useful when the heart rates of studied participants will be below 60 or over 120 beats per minute. Nevertheless, it would be important the development of a smoothing procedure for the L-S spectra, to avoid the picky behavior of the L-S power spectrum.

Heart Rate Variability and Autonomic Regulation in Autism

Leisman G, Melillo R, R Rodríguez-Rojas, Machado C, M Carballo-Barreda, K Batista, JM Morales.

We assessed the autonomic nervous system (ANS) in 20 autistic children and 20 healthy control subjects (paired by age and gender) by heart rate variability (HRV) in two experimental conditions: basal, and watching a cartoon with audio (activated condition). Electrocardiography (ECG) was recorded with the MEDICID-05 with disposable electrodes placed on the chest in positions CM2 and V 5 and using a sampling frequency of 200 Hz. Filters were set for a band spectrum of 0.5-50 Hz. The ECG was recorded in every session for 30 min. Frequency domain HRV indices were calculated with a spectral resolution of $1/420 = 0.00238095$ H, allowing us to study the spectral frequencies from 0.02 to 0.4 Hz, including the VLF band from 0.023 to 0.04 Hz, the LF band from 0.04 to 0.085 Hz, the mid-frequency (MF) band from 0.085 to 0.15 Hz and the HF band from 0.15 to 0.40 Hz. The results of statistical comparisons of both groups demonstrated that in basal records, a significant increment in autistics in frequencies related to parasympathetic activity (SLIDE # 1). Nonetheless, in the activated condition (watching cartoon), a significant decrement of parasympathetic activity was found in autistics, with a predominance of sympathetic function (SLIDE 2).



Cognitive-motor interactions of the basal ganglia in development

Gerry Leisman^{1,2,3,4*}, Orit Braun-Benjamin^{1,2} and Robert Melillo^{1,2,5}

¹ The National Institute for Brain and Rehabilitation Sciences, Nazareth, Israel

² Department of Mechanical Engineering, ORT Braude College of Engineering, Karmiel, Israel

³ ERI, Carrick Institute for Clinical Ergonomics, Rehabilitation, and Applied Neurosciences, Hauppauge, NY, USA

⁴ Facultad Manuel Fajardo, Instituto for Neurology and Neurosurgery, Universidad de Ciencias Médicas de la Habana, Habana, Cuba

⁵ Nazareth Academic Institute, Nazareth, Israel

Edited by:

Ahmed A. Moustafa, University of Western Sydney, Australia

Reviewed by:

Calixto Machado, Instituto of Neurology and Neurosurgery, Cuba
Jorge L. Morales-Quisada, Laboratory of Neuromodulation, USA

*Correspondence:

Gerry Leisman, The National Institute for Brain and Rehabilitation Sciences, ORT Braude College of Engineering, 51 Shunit, PO Box 78, Karmiel 21902, Israel
e-mail: gerry.leisman@staff.nazareth.ac.il

Neural circuits linking activity in anatomically segregated populations of neurons in subcortical structures and the neocortex throughout the human brain regulate complex behaviors such as walking, talking, language comprehension, and other cognitive functions associated with frontal lobes. The basal ganglia, which regulate motor control, are also crucial elements in the circuits that confer human reasoning and adaptive function. The basal ganglia are key elements in the control of reward-based learning, sequencing, discrete elements that constitute a complete motor act, and cognitive function. Imaging studies of intact human subjects and electrophysiologic and tracer studies of the brains and behavior of other species confirm these findings. We know that the relation between the basal ganglia and the cerebral cortical region allows for connections organized into discrete circuits. Rather than serving as a means for widespread cortical areas to gain access to the motor system, these loops reciprocally interconnect a large and diverse set of cerebral cortical areas with the basal ganglia. Neuronal activity within the basal ganglia associated with motor areas of the cerebral cortex is highly correlated with parameters of movement. Neuronal activity within the basal ganglia and cerebellar loops associated with the prefrontal cortex is related to the aspects of cognitive function. Thus, individual loops appear to be involved in distinct behavioral functions. Damage to the basal ganglia of circuits with motor areas of the cortex leads to motor symptoms, whereas damage to the subcortical components of circuits with non-motor areas of the cortex causes higher-order deficits. In this report, we review some of the anatomic, physiologic, and behavioral findings that have contributed to a reappraisal of function concerning the basal ganglia and cerebellar loops with the cerebral cortex and apply it in clinical applications to attention deficit/hyperactivity disorder (ADHD) with biomechanics and a discussion of retention of primitive reflexes being highly associated with the condition.



Persistent Childhood Primitive Reflex Reduction Effects on Cognitive-Motor and Academic Performance in School-Aged Children with ADHD

Robert J. Melillo¹, Gerry Leisman^{2, 1*}, Raed Muallem^{1, 3}, Alon Ornat³

¹The National Institute for Brain and Rehabilitation Sciences, Israel, ²University of Haifa, Israel,

³Oranim Academic College, Israel

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Gross Motor Milestones and Subsequent Development

[Pediatrics](#), June 2016, Akhgar Ghassabian, Rajeshwari Sundaram, Erin Bell, Scott C. Bello, Christopher Kus, Edwina Yeung

Abstract

OBJECTIVE: We examined the longitudinal associations of age at achieving gross motor milestones and children's development in a US cohort of singletons and twins.

METHODS: In the Upstate KIDS study, a population-based study of children born between 2008 and 2010, information on age at achievement of motor milestones and developmental skills was available in 599 children (314 singletons, 259 twins, and 26 triplets). Mothers reported their children's major motor milestones at -4, 8, 12, 18, and 24 months. At age 4 years, children's development was clinically assessed by using the Battelle Developmental Inventory, Second Edition (BDI-2). Primary analyses by using multivariate linear regressions were conducted in singletons. We also examined the associations in twins.

RESULTS: Later achievement of standing with assistance predicted lower BDI-2 scores in singletons in adjusted models (B per SD of age at achievement, -21.9 [95% confidence interval (CI), -41.5 to -2.2]). Post hoc analysis on age of standing with assistance showed that associations were driven by differences in adaptive skills (B = -5.3 [95% CI, -9.0 to -1.6]) and cognitive skills (B = -5.9 [95% CI, -11.5 to -0.4]). Analyses restricted to twins suggested no association between the age at achievement of milestones and total BDI-2 score after adjustment for gestational age and birth weight.

CONCLUSIONS: This study provides evidence that the age of achieving motor milestones may be an important basis for various aspects of later child development. In twins, key predictors of later development (eg, perinatal factors) overshadow the predictive role of milestones in infancy.

References

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Motor Impairment in Sibling Pairs Concordant and Discordant for Autism Spectrum Disorders

[Claudia List Hilton](#) hiltonc@wustl.edu, Washington University in St Louis, USA [Yi Zhang](#) Washington University in St Louis, USA [Megan R. White](#) Washington University in St Louis, USA [Cheryl L. Kiohr](#)

Washington University in St Louis, USA [John Constantino](#) Washington University in St Louis, USA

Abstract

Aim: Although motor impairment is frequently observed in children with autism spectrum disorders (ASD), the manner in which these impairments aggregate in families affected by autism is unknown. We used a standardized measure of motor proficiency to objectively examine quantitative variation in motor proficiency in sibling pairs concordant and discordant for ASD.

Methods: Motor impairment of sibling pairs from 67 ASD-affected families comprising 29 concordant pairings and 48 discordant pairings were assessed using the Bruininks Oseretsky Test of Motor Proficiency, 2nd Edition, a standardized measure of motor proficiency.

Results: Motor skills were substantially impaired among ASD-affected children and highly correlated with autistic severity and IQ, whereas motor skills in unaffected siblings were essentially normal. Total motor composite scores of at least one standard deviation below the general population mean were seen in 83% of the affected group compared with 6% in the unaffected siblings.

Interpretation: Findings indicate that motor impairment constitutes a core characteristic of ASD (not necessarily an ASD endophenotype), which has distinct implications for taxonomy, diagnosis, and approaches to intervention.



The Impact of Maternal Gestational Stress on Motor Development in Late Childhood and Adolescence: A Longitudinal Study.

TGrace T, et al. Child Dev. 2016 Jan-Feb.

Show full citation

Abstract

The number and timing of stressors experienced during pregnancy were investigated using longitudinal data from the Western Australian Pregnancy (Raine) Study cohort (N = 2,900). Motor development data were collected at 10 (n = 1,622), 14 (n = 1,584), and 17 (n = 1,222) years using the McCarron Assessment of Neuromuscular Development. Linear mixed models were used to examine the effect of stress on motor development, accounting for repeated measures. Number of stressful events and mean Neuromuscular Development Index were negatively related ($\beta = -1.197$, $p = .001$). Stressful events experienced in late pregnancy were negatively related with offspring motor development ($\beta = -0.0541$, $p = .050$), while earlier stressful events had no significant impact.

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Larger tonic pupil size in young children with autism spectrum disorder.

Dev Psychobiol. 2009 Mar;51(2):207-11.

Anderson CJ, Colombo J.

Department of Psychology Schiefelbusch, Institute for Life Span

Studies, University of Kansas, Dole Human Development Center, 1000

Abstract

The symptoms of Autism Spectrum Disorder (ASD) have been suggested to manifest from atypical functioning of the autonomic nervous system (ANS), leading to altered arousal and atypical processing of salient stimuli. coherent with this, persons with ASD show heightened autonomic activity, sleep difficulties, and structural and neurochemical alterations within the ANS. Recently, we observed decreased pupil responses to human faces in children with ASD. In the current study, we found differences in baseline (tonic) pupil size, with the ASD group exhibiting a larger pupil size than age-matched controls. Pupil responses are sensitive and reliable measures of ANS functioning, thus, this finding highlights the role of the ANS, and may provide clues about underlying neuropathology.

Atypical Pupillary Light Reflex and Heart Rate Variability in Children with Autism Spectrum Disorder

Chathuri Daluwatte · Judith H. Miles ·
Shawn E. Christ · David Q. Beversdorf ·
T. Nicole Takahashi · Gang Yao

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Abstract We investigated pupillary light reflex (PLR) in 152 children with ASD, 116 typically developing (TD) children, and 36 children with non-ASD neurodevelopmental disorders (NDDs). Heart rate variability (HRV) was measured simultaneously to study potential impairments in the autonomic nervous system (ANS) associated with ASD. The results showed that the ASD group had significantly longer PLR latency, reduced relative constriction amplitude, and shorter constriction/dilation time than those of the TD group. Similar atypical PLR parameters were observed in the NDD group. A significant age effect on PLR latency was observed in children younger than 9 years in the TD group, but not in the ASD and NDD groups. Atypical HRV parameters were observed in the ASD and NDD groups. A significant negative correlation existed between the PLR constriction amplitude and average heart

rate in children with an ASD, but not in children with typical development.

Keywords Pupillary light reflex · Heart rate variability · Autism · Autonomic nervous system

Introduction

Autism spectrum disorders (ASDs) are complex developmental disorders with symptoms in three core areas: social functioning, communication, and restricted or repetitive behaviors. While much progress has been made regarding ASD, the understanding of its etiology is still evolving (Geschwind and Levitt 2007). Although diagnosis of ASD is based on behavioral assessment, various physical mea-



Pupil and salivary indicators of autonomic dysfunction in autism spectrum disorder.

Dev Psychobiol. 2012 May 29.
Anderson CJ, Colombo J, Unruh KE.

Life Span Institute, Neurocognitive Development of Autism Research Laboratory, The University of Kansas,

Abstract

Dysregulated tonic pupil size has been reported in autism spectrum disorder (ASD). Among the possible sources of this dysregulation are disruptions in the feedback loop between norepinephrine (NE) and hypothalamic systems. In the current study, we examined afternoon levels of salivary alpha-amylase (sAA, a putative correlate of NE) and cortisol (used to assess stress-based responses) in two independent samples of children with ASD. We found a larger pupil size and lower sAA levels in ASD, compared to typical and clinical age-matched controls. This was substantiated at the individual level, as sAA levels were strongly correlated with tonic pupil size. Relatively little diurnal variation in sAA taken in the home environment in the ASD group was also observed, while typical controls showed a significant linear increase throughout the day. Results are discussed in terms of potential early biomarkers and the elucidation of underlying neural dysfunction in ASD.



Heart Rate Variability and Autonomic Regulation in Autism

Leisman G, Melillo R, R Rodríguez-Rojas, Machado C, M Carballo-Barreda, K Batista, JM Morales.

We assessed the autonomic nervous system (ANS) in 20 autistic children and 20 healthy control subjects (paired by age and gender) by heart rate variability (HRV) in two experimental conditions: basal, and watching a cartoon with audio (activated condition). Electrocardiography (ECG) was recorded with the MEDICID-05 with disposable electrodes placed on the chest in positions CM2 and V 5 and using a sampling frequency of 200 Hz. Filters were set for a band spectrum of 0.5-50 Hz. The ECG was recorded in every session for 30 min. Frequency domain HRV indices were calculated with a spectral resolution of $1/420 = 0.00238095$ H, allowing us to study the spectral frequencies from 0.02 to 0.4 Hz, including the VLF band from 0.023 to 0.04 Hz, the LF band from 0.04 to 0.085 Hz, the mid-frequency (MF) band from 0.085 to 0.15 Hz and the HF band from 0.15 to 0.40 Hz. The results of statistical comparisons of both groups demonstrated that in basal records, a significant increment in autistics in frequencies related to parasympathetic activity (SLIDE # 1). Nonetheless, in the activated condition (watching cartoon), a significant decrement of parasympathetic activity was found in autistics, with a predominance of sympathetic function