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DEVELOPMENTAL ORIGINS OF HEALTH AND DISEASE

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- Editorial of recent issue *Journal of Child Psychology and Psychiatry* "Developmental neuroscience comes of age," Leckman and March (2011) describe "the phenomenal progress of the past three decades in the developmental neurosciences."
- "Over the past decade it has…become abundantly clear that…the in utero and immediate postnatal environments and the dyadic relations between child and caregivers within the first years of life can have direct and enduring effects on the child's brain development and behavior."

- “Indeed, the enduring impact of early maternal care and the role of epigenetic modifications of the genome during critical periods in early brain development in health and disease is likely to be one of the most important discoveries in all of science that have major implications for our field.”
- “A scientific consensus is emerging that the origins of adult disease are often found among developmental and biological disruptions occurring during the early years of life.”

- Echoing this and with an eye to early prevention, in current psychiatric literature Insel and Fenton (*Archives of General Psychiatry*, 2005) articulate widely held principle, “Most mental illnesses…begin far earlier in life than was previously believed.”
- Early intervention: recent approaches integrating neuroscience and pediatrics now focusing on reducing significant stress and adversity in the early periods of childhood (Shonkoff, Boyce, & McEwen, *Journal of the American Medical Association*, 2009).

- In this talk suggest that these significant advances in developmental science directly impact and update pediatric practice.
- Schore (2005, *Pediatrics in Review*):
- “Updated models of early development which integrate developmental neuroscience, developmental psychology, developmental biology, and child psychiatry have direct relevance to pediatrics’ interests in the normal and abnormal functions of the developing child’s mind and body.”

- Oxford dictionary defines pediatrics as “the branch of medical science that deals with childhood and the diseases of children.”
- Field specializes in the diseases that are commonly found in the early stages of human development that are characterized by active states of growth.
- We know that the biology of growing tissues and the psychology of an immature yet evolving mind and body are qualitatively different than a mature organism.

- Infant's immature immune system particularly vulnerable to pathogens that assault developing organs, as well as to psychopathological forces that threaten developing brain-mind-body systems.
- Despite different origins of these stressors both trigger common adaptive and maladaptive alterations of an immature organism's evolving psychobiological coping mechanisms in order to respond to internal pathogenic organisms and external psychopathogenic forces.

- Definition of the medical specialty of pediatrics also states essential interest in not just diseases of children but in “childhood”, stage of development before maturation, before adulthood.
- Clear implication is that normal healthy processes of development are also an essential part of knowledge base of pediatrics.
- Research in developmental biology and physiology now strongly supports a model of the “developmental origins of *health and disease*” (Gluckman & Adler, *Science,* 2004).

- This recent information on developmental origins of health and disease can be translated directly into clinical practice. These advances are directly relevant to pediatricians' interest in normal and abnormal functions of the developing child's mind and body.
- Common ground of expanding knowledge in developmental sciences can strengthen ties of pediatrics to allied fields that border it: pediatric neurology, child psychiatry and psychology, developmental psychology, and infant mental health.
- Schore plenary to American Psychological Association (2009): this expanding knowledge is generating a paradigm shift across disciplines.

- Schore (2005): ongoing paradigm shift in basic and applied sciences expressed in 3 converging themes.
- First arises from wealth of neurobiological data available since last decade, the “decade of the brain.” Contemporary neuroscience is very interested in the brain growth spurt (last trimester through 2nd year); early development of right brain in this critical period.
- Updated models of attachment theory that emphasize interpersonal neurobiology and emotional and social functions now interfacing with developmental neuroscience studies of early developing right brain dominant for processing emotion.

- Second theme of paradigm shift seen in transformations within psychology, psychiatry, and neuroscience from cognition to emotion.
- Ryan (*Motivation and Emotion*, 2007): “After three decades of the dominance of cognitive approaches, motivational and emotional processes have roared back into the limelight.”
- Interdisciplinary developmental research suggests that the evolutionary mechanism of creation of an attachment bond of social-emotional communication, the maturation of affects, and the attainment of adaptive capacity for the self-regulation of affect represent the key events in infancy.

- Third theme of paradigm shift revolves around one of the few theoretical constructs that lies at the core of literally every biological and psychological discipline – self-regulation.
- The process of development represents a progression of stages in which emergent adaptive self-regulatory structures and functions enable qualitatively new and more complex interactions between the individual and the social environment.
- Self-regulation tied to affect regulation.

- Three trends of paradigm shift - studies of early right brain development, emphasis on attachment and processing of social-emotional information, and focus on self-regulation - converging to produce clinical models that are directly relevant to pediatrics, specifically, models of the origins of the development of childhood mental health and mental illness.
- The mission statement of the American Academy of Pediatrics states its commitment to “the attainment of optimal physical, mental, and social health for all infants, children, adolescents, and young adults.”

- With this introduction in mind, in following use perspective of Schore's regulation theory to discuss recent studies of the experience-dependent maturation of the "emotional" "social" right brain, the interpersonal neurobiology of attachment, and the development affect regulation.
- Suggest that development of self-regulation is central to emergence of infant social-emotional, mental, and physical health, and that current information from developmental neuroscience is relevant to interests of pediatrics in normal and abnormal functions of developing child's mind and body.

Affect Regulation and the Origin of the Self

The Neurobiology of Emotional Development

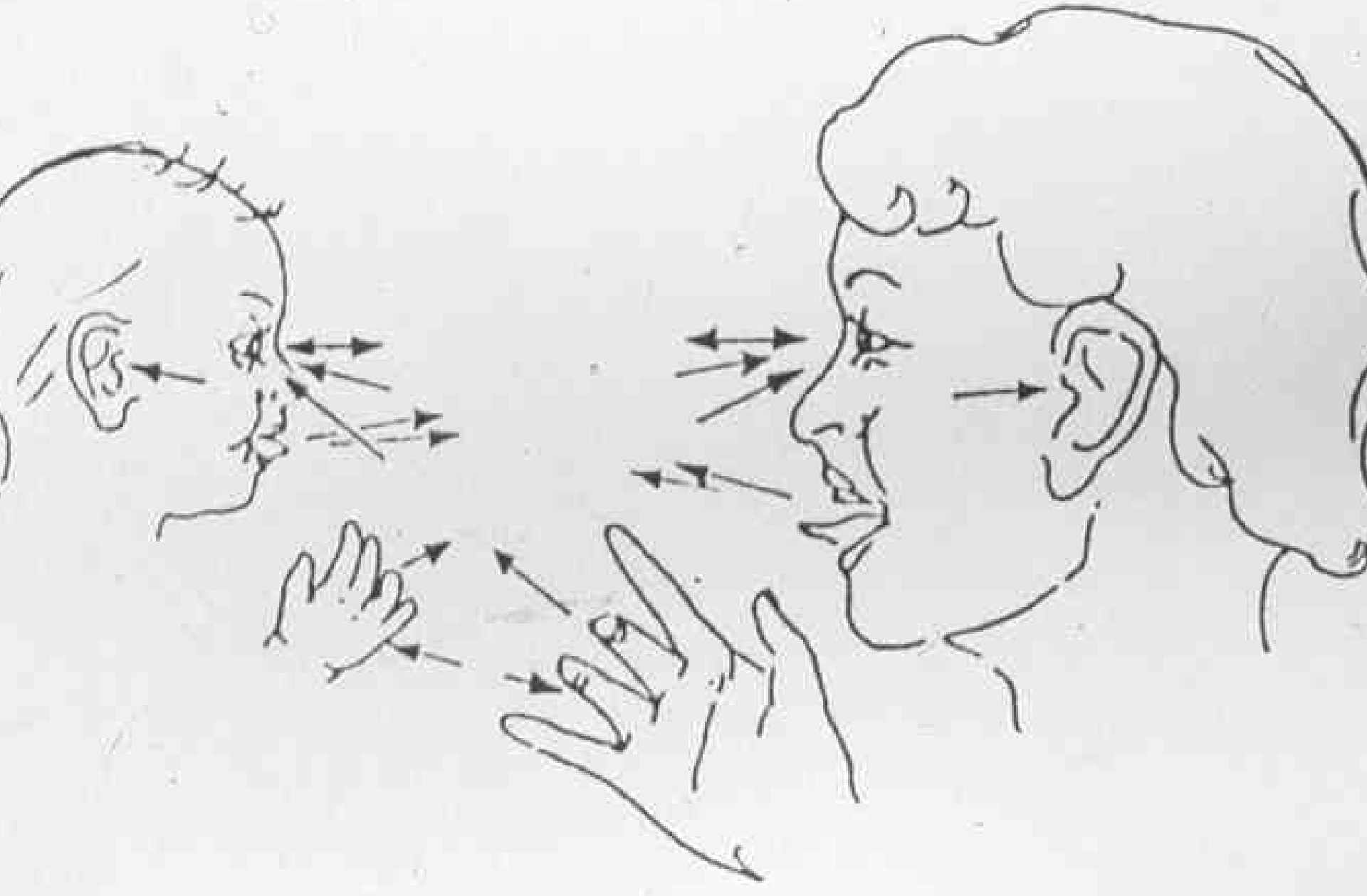
Allan N. Schore

- Leckman and March (2011): “A complex, dynamic story is unfolding of evolutionarily conserved genetic programs that guide mammalian brain development and how our *in utero* and our early postnatal interpersonal worlds shape and mold the individuals (infants, children, adolescents, adults and caregivers) we are to become.”
- Prenatal and postnatal epigenetic factors in social environment that impact genome created within mother- infant attachment relationship.

- Schleussner et al. (*Early Human Development*, 2004) report “an earlier maturation of certain right than homologous left hemispheric brain areas during fetal brain development.”
- Kasprian et al. (*Cerebral Cortex*, 2010): “The prenatal origin of hemispheric asymmetry: an *in utero* neuroimaging study.” 26 gestational weeks fetuses right superior temporal sulcus appears earlier and is deeper than left.
- “Our structural data further support the findings of functional neuroimaging studies indicating an earlier maturity of right hemispheric function.”

- Walker-Andrews & Bahrick (*Infancy*, 2001):
- “From birth, an infant is plunged into a world of other human beings in which conversation, gestures, and faces are omnipresent during the infant’s waking hours. Moreover, these harbingers of social information are dynamic, multimodal, and reciprocal.”
- Brown and Jaffe (*Neuropsychologia*,1975): “The right hemisphere can be considered dominant in infancy, for the type of visual and acoustic communication which is relevant for the prelinguistic child.”

- Bowlby (1969): mother-infant attachment communications are “accompanied by the strongest of feelings and emotions, and occur within a context of “facial expression, posture, tone of voice, physiological changes, tempo of movement, and incipient action.”
- Schore (1994): during episodes of *visual-facial, auditory-prosodic*, and *tactile-gestural* affective communications, psychobiologically attuned caregiver’s behavior is contingent, easily predictable, and manipulatable by the infant.



- Schore principle of interpersonal neurobiology: “The self-organization of the developing brain occurs in the context of another self, another brain.”
- In these right brain-to-right brain experiences infant becomes securely attached to psychobiologically attuned caregiver who minimizes negative affect and maximizes positive affect.
- Brancucci et al. (*Proc. Royal Soc. London B*, 2009): “The neural substrates of the perception of *voices, faces, gestures, smells, and pheromones*, as evidenced by modern neuroimaging techniques, are characterized by a general right-hemispheric functional asymmetry.”

- RH visual-facial attachment communications
- Tzourio-Mazoyer et al. (*NeuroImage*, 2002): PET study of 2-month-old infant looking at image of a woman's face; activation of infant's RH.
- Grossmann et al. (*Social Cognitive and Affective Neuroscience*, 2007): 4-month-old infants presented with images of a female face gazing directly ahead show enhanced gamma electrical activity over right prefrontal areas.
- Nakato et al. (*Human Brain Mapping*, 2009): near-infrared spectroscopy research reveals 5-month-olds' RH responds to images of adult female faces.

- RH auditory-prosodic attachment communications
- Homae (*Neurosci. Res.*, 2006): “Prosodic processing in 3-month-old infants is subserved by the right temporoparietal region.”
- Telkemeyer et al. (*J. Neurosci.*, 2009): NIRS of 2-6 day neonates show “responses to slow acoustic modulations are lateralized to the right hemisphere.”
- Mento et al. (*Eur. J. Neurosci.*, 2010): EEG study of auditory pitch processing in preterm infants born at 30 gestational weeks: “These findings suggest that the earlier right structural maturation in foetal epochs seems to be paralleled by a right functional development.”

- RH auditory-prosodic attachment communications
- Grossmann et al. (*Neuron*, 2010): “The developmental origins of voice processing in the human brain.”
- NIRS study of emotional prosody. 7-month-old infants respond to emotional voices in a voice-sensitive region of the right superior temporal sulcus. Happy prosody activates the right inferior frontal cortex.
- “The pattern of finding suggests that temporal regions specialize in processing voices very early in development and that, already in infancy, emotions differentially modulate voice processing in the right hemisphere.”

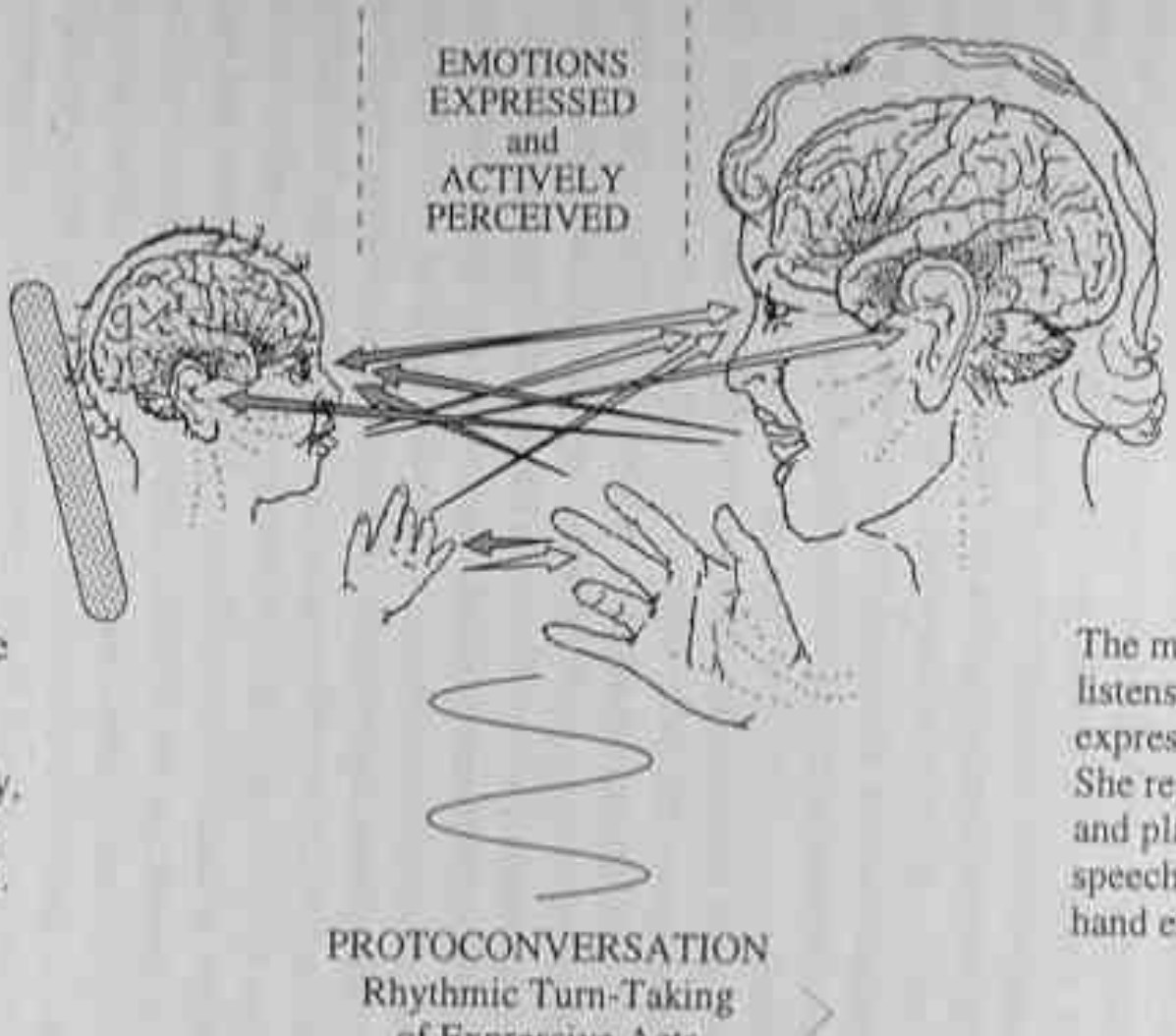
- RH tactile-gestural attachment communications
- Sieratzki & Woll (*Behav. Brain Sci.*, 2005) on touch and RH: “The emotional impact of touch, the most basic and reciprocal mode of interaction is also more direct and immediate if an infant is held to the left side of the body.”
- Nagy (*Infant Child Develop.*, 2006): study human neonates in their first 3-96 hours of life, and find a “lateralized system for neonatal imitation.”
- “The early advantage of the right hemisphere (Chiron et al.,1997; Schore, 2000; Trevarthen, 2001) in the first few months of life may affect the lateralized appearance of the first imitative gestures.”

- RH tactile-gestural attachment communications
- Montirosso, Borgatti, & Tronick (2010): observe left-sided regulatory gestures when infant stressed.
- “Infants cope with the emotional distress caused by unresponsive mothers through self-regulation behaviors associated with a greater activation of the right hemisphere. In sum, this finding supports the view that during a stressful condition there is a state-dependent activation of the right hemisphere.”
- “More generally these findings suggest that the right hemisphere is more involved in the social and biological functions regarding infant caregiver emotional bonding (Schore, 2005; Siegel, 1999).”

- McGilchrist (2009): “The right hemisphere, is…more closely in touch with emotion and the body (therefore with the neurologically ‘inferior’ and more ancient regions of the central nervous system)…”
- To regulate infant’s right brain, crescendos /decrescendos mother's affective state in resonance with similar crescendos/decrescendos of infant’s internal states of positive and negative arousal.
- Winnicott (1986): “The main thing is a communication between the baby and the mother in terms of the anatomy and physiology of live bodies.”

- Ovtscharoff & Braun (*Neuroscience*, 2001):
- “The dyadic interaction between the newborn and the mother constantly controls and modulates the newborn’s exposure to environmental stimuli and thereby serves as a regulator of the developing individual’s internal homeostasis.
- The regulatory function of the newborn-mother interaction may be an essential promoter to ensure the normal development and maintenance of synaptic connections during the establishment of functional brain circuits.”

Primary Inter-Subjectivity



The baby, attracted to the mother's voice, face expressions and hand gestures, replies playfully, with affection: imitating, and provoking imitations.

The mother watches a
listens, anticipating th
expressions intuitively
She replies sympathet
and playfully, with 'm
speech, touches and fa
hand expressions

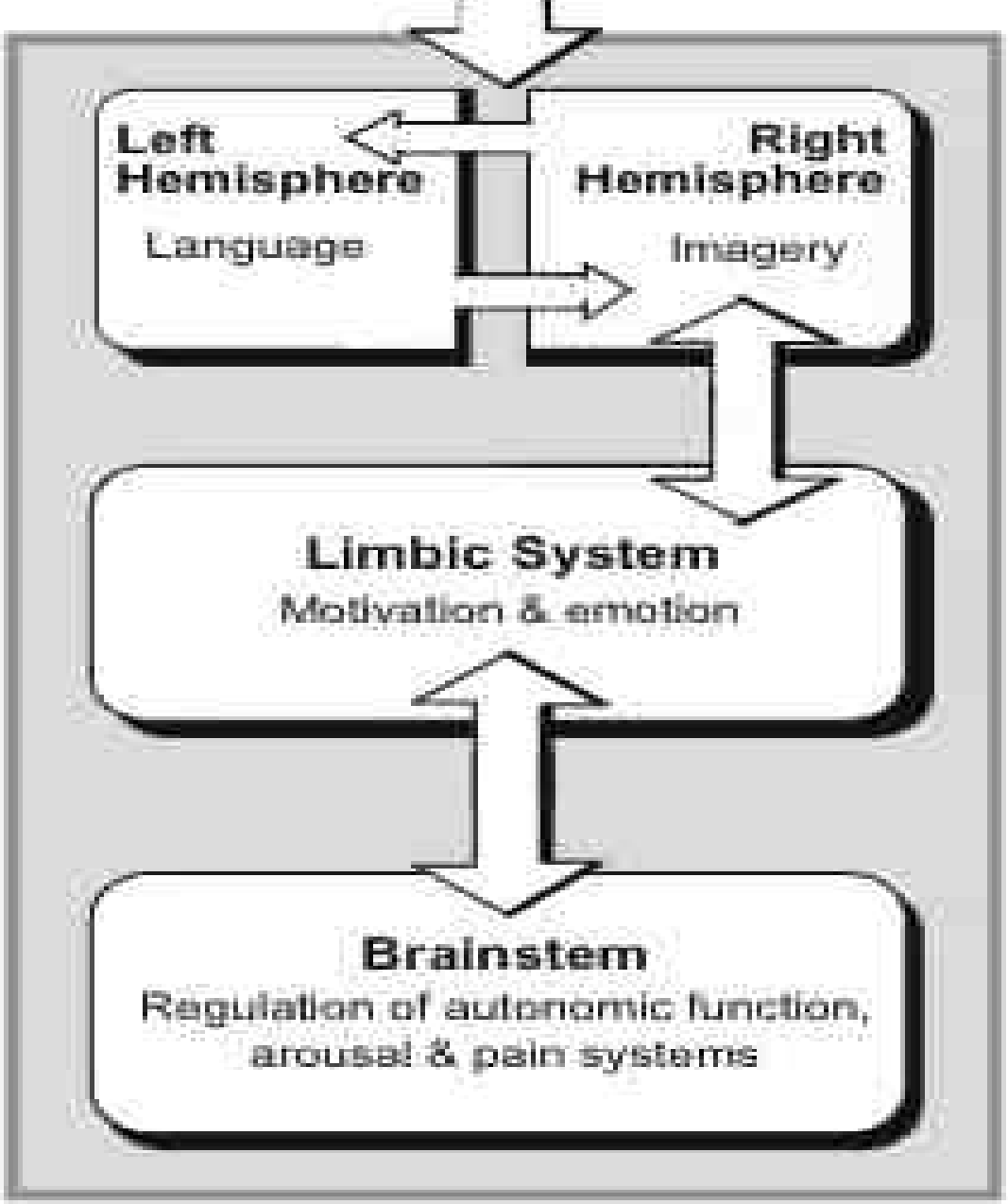
PROTOCONVERSATION
Rhythmic Turn-Taking
of Expressive Acts

- Lagercrantz & Ringstedt (*Acta Pediatr.*, 2001): in prenatal and postnatal periods rate of synaptogenesis estimated at 40,000 new synapses every second.
- Knickmeyer et al. (*J. Neuroscience*, A structural MRI study of human brain development from birth to 2 years, 2008): “Total brain volume increased 101% in the first year, with a 15% increase in the second… These was a robust growth of the human brain in the first two years of life.”
- “The volume of the subcortical area (including brainstem) increased by 130% in the first year and by 14% in the second year.”

- Schore (1994): attachment impacts developing RH.
- Sieratzki & Woll (*Lancet*, 1996): “The role of the right hemisphere is crucial in relation to the most precious needs of mothers and infants.”
- Chiron et al. (*Brain*, 1997): “The right brain hemisphere is dominant in human infants.”
- Allman (2005): “The strong and consistent predominance for the right hemisphere emerges postnatally.”
- Howard & Reggia (*Brain and Cognition*, 2007): “Earlier maturation of the right hemisphere is supported by both anatomical and imaging evidence.”

- Lenzi et al. (*Cerebral Cortex*, 2009): fMRI study of mother-infant emotional communication offer data "supporting the theory that the right hemisphere is more involved than the left hemisphere in emotional processing and thus, mothering."
- Minagawa-Kawai (*Cerebral Cortex*, 2009): near-infrared spectroscopy study of infant-mother attachment at 12 months, "our results are in agreement with that of Schore (2000) who addressed the importance of the right hemisphere in the attachment system."

- Schore (1994): bodily-based attachment transactions imprint right brain, which is deeply connected into emotion processing limbic system and ANS.
- Helmeke et al. (*Neuroscience*, 2001): “The functional maturation of limbic circuits is significantly influenced by early socio-emotional experience.”
- Dapretto et al. (*Nature Neuroscience*, 2006): “Typically developing children can rely upon a right hemisphere-mirroring neural mechanism - interfacing with the limbic system via the insula - whereby the meaning of imitated (or observed) emotion is directly felt and hence understood.”


Left
Hemisphere
Language
Right
Hemisphere
Imagery
Limbic System
Motivation & emotion
Brainstem
Regulation of autonomic function,
arousal & pain systems

- Gunnar (2000): maternal care within attachment relationship shapes the infant's hypothalamic-pituitary-adrenocortical (HPA) axis.
- Wittling et al. (*Acta Physiologica Scand.*,1997): RH regulates HPA and mediates human stress response; RH central to the control of vital functions supporting *survival* and enabling the organism to cope with stresses and challenges.
- Sullivan & Dufresne (*Brain Research*, 2006): Optimal stress regulation is dependent on "right hemispheric specialization in regulating stress - and emotion-related processes."

- Subsequent to child's formation of an attachment to mother in 1st year, forms another, to father in second.
- "The biorhythmicity of man with infant and woman with infant" affords the infant to have "interactive, state-sharing, and state-attuning experiences with two different kinds of caregivers" (Herzog, 2001).
- Braun's laboratory here in Germany published series of studies demonstrating that paternal care affects synaptic development of the developing brain.
- Father critically involved in male and female toddler's aggression regulation [vs. mother and fear regulation]
- Right hemisphere ends initial growth spurt in middle/end of second year, as left hemisphere begins its own

- For rest of life span, right brain encodes, in implicit-procedural memory, internal working model of attachment, strategies of affect regulation that nonconsciously guide individual through various affectively charged interpersonal contexts.
- In all later interpersonal functioning this RH representation of attachment, acting at levels beneath conscious awareness, is accessed to appraise, interpret, and regulate socioemotional information and thereby guide future action in familiar and novel interpersonal environments.

- Attachment = dual processes of right brain implicit bodily-based self-regulation:
- *Interactive regulation*, ability to resiliently regulate emotional states through interactions with others in interconnected contexts (intersubjectivity). Strategy of "open and direct communication of intentions and feelings together with negotiation and compromise."
- *Autoregulation*, regulation of internal psychobiological states in autonomous contexts, without others.
- Secure attachment = adaptively shift between 2 modes, depending upon context.
- Tension between 2 regulatory strategies responsible for conflict between interconnectedness and autonomy

- Uddin (*SCAN*, 2006): “The emerging picture from the current literature seems to suggest a special role of the RH in self-related cognition, own body perception, self-awareness and autobiographical memories”
- Schutz (*Neuropsychology Review*, 2005): “The right hemisphere operates a distributed network for rapid responding to danger and other urgent problems. It preferentially processes environmental challenge, stress and pain and manages self-protective responses such as avoidance and escape.”
- These adaptive right brain functions are initially imprinted in right brain-to-right brain affective communications during critical periods of infancy.

- Attachment impacted RH adaptive functions:
- Nonverbal processing of facial expressions, prosody, gestures.
- Regulation of central and autonomic arousal.
- Storage of implicit/procedural emotional memory.
- Processing novelty, threat, and unexpected stimuli.
- Regulation of HPA and SAM axes and cortisol release.
- Control of vital functions supporting survival; enabling organism to cope actively and passively with stress.
- Reception, expression, and communication of negative affects and pain.
- If attachment traumatic, these functions impaired.

AFFECT DYSREGULATION

AND DISORDERS OF THE SELF

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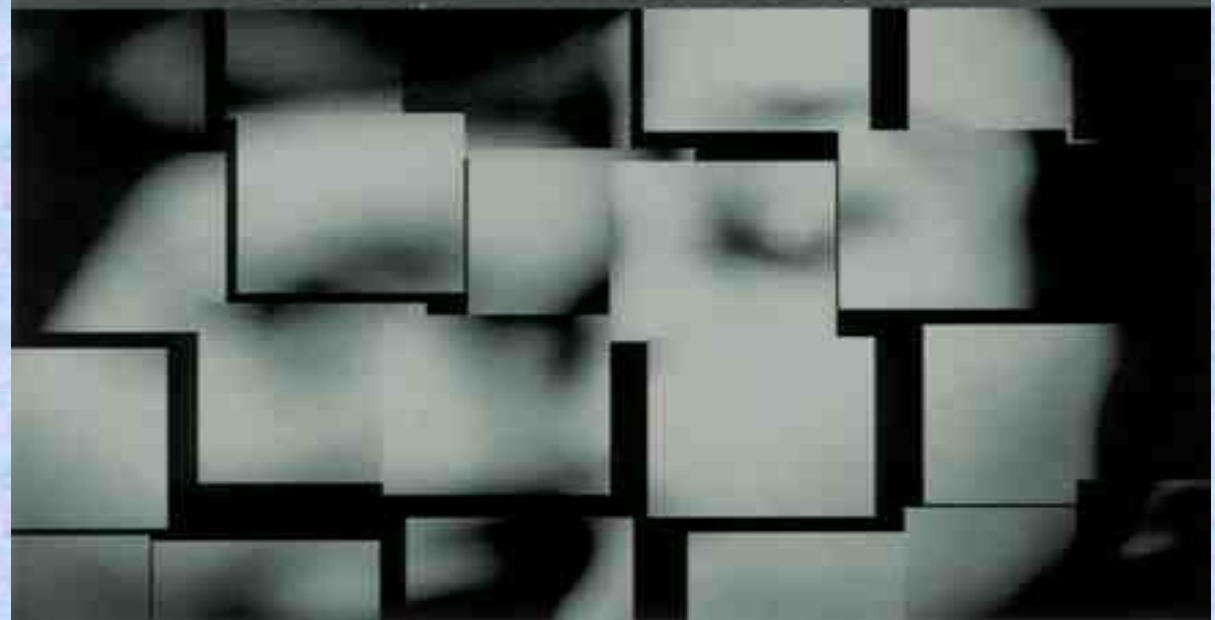

- Helmeke et al. (*Cerebral Cortex,* 2001): “Positive (formation of emotional attachment) or negative (e.g., maternal separation or loss) emotional experience may carve a permanent trace into a still developing neuronal network of immature synaptic connections, and thereby can extend or limit the functional capacity of the brain during later stages of life.”
- Schore (*Australian New Zeal. J. Psychiatry,* 2002): early relational trauma (abuse/neglect) associated with severe attachment stressors and impaired right brain development.

- Recall, “Most mental illnesses…begin far earlier in life than was previously believed.”
- Schore (1994-2011) insecure attachments associated with altered maturation of right orbital prefrontal cortex and deficits in affect functions and stress regulation.
- Altered development of OFC in schizophrenia; autism; affective psychosis; bipolar disorder; borderline personality disorder; psychopathic personality disorder, aggression, and violence; alcohol and drug addiction; posttraumatic stress disorder; dissociative identity disorder; panic disorder; depression.

- Felitti & Anda (2010): history of relational trauma at risk for not only psychiatric but medical disorders
- Shirtcliff, Coe, & Pollak (*PNAS*, 2009): “Early childhood stress is associated with elevated antibody levels to herpes simplex virus type 1.”
- Danese et al. (*PNAS*, 2007): “Childhood maltreatment predicts adult inflammation in a life course study.”
- Batten et a. (*J. Clin. Psychiatry*, 2004): “Childhood maltreatment as a risk factor for adult cardiovascular disease and depression.”
- Picardi et al. (*Psychosomatic Med.,* 2009): attachment avoidance associated with lower Natural Killer cell cytotoxicity.

- Schore (2010) Synopsis. *The Impact of Early Life Trauma on Health and Disease: The Hidden Epidemic*.
- “Recent models of early life trauma are altering their focus from deficits in later maturing conscious, verbal, explicit and voluntary behavior, to impairments of early maturing nonconscious, nonverbal, implicit and automatic adaptive social emotional functions.
- Developmental neuroscience is now moving from studies of later maturing left brain conscious verbal cognitive processes into the early preverbal development of adaptive emotion processing right brain systems in pre- and postnatal periods.”

- Schore & Newton (in press): *Diagnostic Implications Clinical Application of Regulation Theory: Early Attachment Interventions.*
- Assessments of infant mental health and social-emotional development in first year must evaluate right brains of both members of an attachment dyad
- In the first two years evolving right lateralized *visual-facial, auditory-prosodic, and tactile-gestural* functions of "the human social brain" can be assessed over the pre- and postnatal stages of infancy to appraise the ongoing status of emotional and social development.

- Mento et al. (*Eur. J. Neurosci.*, 2010):
  "The RH would sustain the functions necessary for the survival of the species, such as *visuospatial or emotional processes*. Consequently the earlier and faster development of the neural substrates underlying these functions is needed to prevent possible impairment during infancy and childhood."
- Grossmann et al. (*Neuron*, 2010): in postnatal periods, "responses to *voices and emotional prosody*…might thus serve as one of potentially multiple markers that can help with an early identification of infants at risk for neurodevelopmental disorders."

- Montirosso et al. (2010): call for study of different *gestures* with simultaneous measurement of brain functions." "Such studies would also be useful with samples of high risk-infants whose behavior and brain organization may be compromised."
- Evaluation of right lateralized nonverbal emotional communication and affect regulation could be used diagnostically as markers of attachment development, complexity of right brain maturation, infant mental health, and targets of early relational intervention.

- Schore (*Infant Mental Health J.*, 2001):
- "*Adaptive* infant mental health can be fundamentally defined as the earliest expression of efficient and resilient strategies for coping with novelty and stress, and *maladaptive* infant mental health as a deficit in these same coping mechanisms."
- "The former is a resilience factor for coping with psychobiological stressors at later stages of the life cycle, the latter is a risk factor for interruptions of developmental processes and a vulnerability to the coping deficits that define later-forming psychopathologies."

- Ongoing paradigm shift: psychobiological markers that assess attachment relationships, right brain development, affect regulation, and infant mental health need to be included in diagnostic armamentarium of the practicing pediatrician.
- This knowledge allows the clinician to more deeply understand the system of nonverbal communication and interactive regulation that lies at the core of the mother-infant relationship, the fundamental element of a healthy child's brain/mind/body developmental matrix.

- Recall, current science is actively investigating the "developmental origins of *health and disease*" (Gluckman & Adler, *Science,* 2004).
- Infant Mental Health Task Force of Zero to Three (2001): "Infant mental health is the developing capacity of the child from birth to three to experience, regulate, and express emotions; form close interpersonal relationships; and explore the environment and learn…Infant mental health is synonymous with healthy social and emotional development."

- World Association for Infant Mental Health now stresses “infant social-emotional development, caregiver-infant interactions, contextual and cultural influences on infant and family development, and all conditions that place infants and/or their families at risk for less than optimal development.”
- Early social-emotional development lies at core of pediatrics’ commitment to “the attainment of optimal physical, mental, and social health for all infants, children, adolescents, and young adults.”
- I propose due to recent advances in developmental sciences pediatrics is now in a position to update its models of early intervention and prevention.