ISSN 1188-3936 www.ddd.uwo.ca

Schulich MEDICINE & DENTISTRY Western

The Clinical Bulletin

of the

Developmental Disabilities Division

Vol 24 – No 1 **Spring 2013**

Brain Development: Neurobehavioral Perspectives in Developmental Disabilities

Children and adults with developmental (intellectual) and learning difficulties may exhibit delayed cognitive development.

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[A revised and updated version of "*Brain Development: Neuro-Behavioral Perspectives in Developmental Disabilities*" by Jay Rao, was published in October 2012. This revised version is reprinted with permission of www.intellectualdisability.info whose ethos is *"An understanding of the nature of intellectual disability is essential for health care professionals, who are required to support equal access to their services for all disabled people."]*

One of the most frequent reasons for referring a person with developmental disability to a hospital or a clinic is aggression and self-injurious behaviours. Such behaviours are not only distressing to the individual, but are also challenging to the care provider. Unfortunately, quite often, there is no clear understanding of the reasons for the crisis, which inevitably leads to less than optimal interventions.

There are often multiple factors associated with such behaviours which are frequently viewed as maladaptive in nature. A number of biomedical issues, developmental factors, sensory modulation difficulties, communication problems, emotional experiences and environmental stressors can have a significant impact on a person's ability to cope. In this article, I will briefly discuss how certain regions of the brain regulate behaviour and emotions, how these regions develop, and the various influences that shape their development. A brief discussion of these neuro-developmental events helps in the understanding of the regulatory systems in the brain and why disruption to these will lead to behavioural and emotional dysregulation.

EXECUTIVE FUNCTIONS

Executive functions are a set or domains of functions which regulate, and manage behaviours, emotions and certain cognitive processes. They are important for problem-solving, self-awareness and directive functions. A well functioning executive system is crucial for adaptation to the environment especially if novel situations or problems have to be dealt with.

The ***executive brain*** is made up of the *frontal system*, which includes the frontal lobe of the brain, but not exclusively. The frontal lobe is at the helm of a closely interconnected network which includes many cortical and subcortical regions. It is connected with the 'emotional brain' or the limbic system, the 'attention and arousal brain', the reticular activating system, the 'processing network' for sensory perception, memory and other cognitive processes. It is also connected with the cerebellum, thalamus and striate region concerned with sensory-motor activity and in synchronicity. There is also a network of connections within the frontal lobe, and interconnections with the other hemisphere of the brain.

The executive brain develops in the last three months (approximately) of pregnancy, and continues to develop over the next two years, post-birth and further. During this time, the brain size of the baby is 50% larger than that of the adult. Normally from two years to puberty, the most used 'wiring' is retained and the others are 'pruned'. By puberty, the brain size approximates the adult size.

During the development of the executive brain, there is intense activity in the cortex, with the neurons migrating to their pre-programmed layers, with their maturation, and the establishment of their intricate connections. The brain, at this stage, is very vulnerable to damage and the disruption of connections.

Example of autism

We know a great deal about the development of the brain in autism. Research has indicated that in autism there are abnormalities in many aspects of the development of the cortex. The brain size, which is larger in the first two years post-birth, reduces gradually from two years onwards, in normally developing children. *In contrast, autistic children who are two to four years of age have larger brain volume*. *Such persistence of increased brain size may indicate aberrant development within the cortex or failure to prune excessive connections.*

There is the possibility that the increase in size may be accompanied by abnormal 'bundling' of neurons called 'mini columns'. Instead of a wide and functional network of 'wires' in the cortex, one may find an *array of neurons* in layers II to VI of the cortex; of *interneurons* (which are short wires that connect neurons within a region) in layers I to VI of the cortex; and of dendrites and axons (*dendrites* are hair-like wires that spring from the head of the neuron and connect with other neurons; and *axons* are the elongated tail of the neuron that connects with other neurons to form continuous wiring).

Such long and short connecting wires are gathered in bundles or “mini columns”, which are then packaged as “macro columns”.

In autism, these mini- and macro- columns are narrower in width, have smaller neurons, and have reduced neuropil space (interwoven matrix of dendrites and axons). In addition, the balance between the inhibitory (braking system) and the excitatory connections may be disturbed as well.

The other problem is in that the *regional connection is abnormal*. To explain, normally, each lobe of the brain, such as the temporal, the frontal, the parietal, and the occipital are clearly *demarcated* from each other. ***In autism, the demarcation (boundaries) between frontal and temporal lobes is poor***. The result is that there are intense connections between these two lobes, exclusively. ***Consequently, or simultaneously, the long connections that are necessary between the frontal lobe and the parietal lobe, posterior lobes etc. are affected (reduced). Frontal and Temporal lobe development is stunted at an early stage leading to lack of differentiation, which then leads to hyper-connectivity between these areas, and under-connectivity and block to coherence development with other critical brain regions.***
Such abnormal connectivity in the executive brain leads to poor processing of emotional, cognitive, perpetual and attentional inputs, as well as language functions.

The discussion so far highlights the precise and delicate nature of the development of connections in the brain and the profound effects on the executive brain architecture that any disruptions in the process can have.

Domains of executive function and the behavioural consequences of dysfunction:

Broadly, executive functions can be divided into those that regulate behaviour and emotions, and those that are concerned with meta-cognitive functions (problem-solving). The first category of behaviour and emotion regulation indices includes at least ***4 domains***:

1. **Inhibition** - This is the *braking system* that regulates behaviours. If this domain is dysfunctional, one may notice explosive behaviours, or aggressive, self-injurious behaviours that are disproportionate to the trigger.

2. **Shift** – Our ability to ‘shift’ mental sets enables us to be flexible. If this is dysfunctional, we may become *rigid, perseverative, repetitive,* and unable to extricate ourselves from the ‘loop’.

3. **Emotional regulation** – Any dysfunction in this domain leads to lability of mood, rapid changes in mood and excessive emotional reaction to situations.

4. **Self-monitor** – Self-monitoring is an important function, which enables us to be aware of our 'minute to minute' state of emotions and behaviours. Such feedback is crucial in regulating behaviours.

5. **Metacognitive domains** – These are a collection of domains concerned with problem-solving. Central to this is the domain of 'working memory', which enables us to hold information 'on-line', so that we can carry out an action or intention, or even carry on a conversation.

Some of the research that has been done to assess executive functions in those with developmental disabilities and behavioural challenges, including our own work, has demonstrated significant executive function deficits in individuals with developmental disabilities who are referred for treatment of aggressive and self-injurious behaviours. In our (unpublished) work, *Shifting* seems to be most affected in a heterogeneous group of developmentally disabled adults with behavioural issues. All other domains such as Inhibition, Emotional Regulation and Working Memory are also significantly affected.

In normal development, the brain, having 'pruned down' to a smaller adult size by puberty, goes through another phase of frenzied development. This involves intense activity of the neurons connecting with each other through their dendrites. **They form highly connected networks that multiply the brain's computing power.**

In autism, there is significant failure in the maturity of such circuitry, leading to the emergence of new or intensified deficits in Frontal Lobe skills. Executive functions, working memory and social-communication skills are negatively affected.

Some recent research shows that the connectivity of the different localities of the brain is abnormal suggesting from a cellular and molecular perspective that pruning may be decreased in autism. This leads to the network of connections in the brain favouring short-range connections over long-range connections. As a result, the brain cannot integrate information efficiently. In autism, information is processed *locally*, instead of being sent out to a wider *net work* in the brain. As the authors of this study indicate, no 'hub' plays a specific role in information flow, but rather Information flows along redundant routes to get from point A to point B. The brain responds in the same rigid way to many different situations as a result (Peters J.A., Taquet M et al, BMC medicine, 2013). Others have recently found that in the autistic brain, in the Cingulate region which is an important component of the Executive system, the neurones were less connected with other parts of the brain, and the cingulate 'bundles' were smaller (Owen J P, Li Y, et al, NeuroImage, 2013). This leads to poor adaptation to the environment and life demands *as people grow into their adulthood.*

The implications are that the behavioural challenges, poor adaptation, and emotional dysregulation in persons with developmentally disabilities, may be consequential to the dysfunction in the frontal executive system. **Any planned behaviour intervention has to take into account these underlying developmental factors in order to be successful.**

SOCIAL BEHAVIOUR

Appropriate social interactions and behaviour are essential in maintaining our effectiveness in day-to-day functioning. Several skills are necessary to maintain social competence. The ability to communicate is important, but as necessary are the abilities to imitate, observe, and understand the intentions of others, both in communication and in actions. A well-developed Theory of Mind (understanding the other person's state of mind and emotions) is crucial in any successful, empathetic interaction with others. In autism, many of these essential social skills, such as the ability to imitate, and understand the other person's emotions and intentions are not well developed. Research, especially imaging studies, has pointed to a system of neurons known as the 'mirror neurons'. These are dysfunctional in autism. The mirror neuron system in the frontal lobes is active when the person is observing another person's gestures, expressions, and actions. The system 'imitates' these, as though in rehearsal. It is also active during the process of understanding intentions behind actions and emotions. Along with the Limbic system (emotional brain), the mirror neuron system helps understand the feeling of others at an emotional level. Unfortunately in autism, given the dysfunction of the mirror neurons, the person may experience difficulties in social situations.

Sensory modulation/regulation disorders

Sensory modulation disorders are also important determinants of challenging behaviours. An individual who has an inability in sitting still, and is rocking, bouncing and constantly moving may not have ADHD, but may have difficulties with proprioceptive sensations (feeling the position of body in space, muscle tone and joint sensation). In autism, studies have revealed multimodal sensory integration problems such as visual, vestibular, and position sense, underscoring the broad brain connectivity problems affect information integration (Minshew & Williams).

An individual with a low threshold for certain decibels of sound may become agitated by background noises such as that of a refrigerator motor or an air conditioner. The noise from a washing machine or a vacuum cleaner may trigger agitation. Similarly, processing touch and temperature sensations may be unusual because of high or low threshold.

Given that the sensory system is the mediator between us and the world outside, and the fact that we constantly try to maintain equilibrium in spite of the constantly changing environmental inputs, an intact, and efficiently regulated sensory system is of crucial importance in establishing a zone of comfort. Modulation difficulties can, therefore, have serious consequences to our adjustment to the world and will inevitably lead to discomfort and agitation. *In persons who additionally have poor problem-solving skills, this may lead to significant frustration, as they have little ability to find alternatives.*

Communication disorders

Communication disorders have a significant negative impact on the ability of an individual to cope in a communicatively demanding (for the individual) environment. For example, in autism, there is significant disturbance in the organization of neural circuitry

in the language processing areas. As stated earlier, local circuitry (between frontal and temporal lobes) persist, and are overdeveloped, instead of the *development of wide-spread functional connections in the brain*. The temporal lobe processes auditory input. It specifically processes words and enables us to receive and comprehend speech. The frontal lobe is the expressive language area. The ability to form sequential ideas and express thoughts as language is a frontal lobe function. The connections between the frontal and temporal regions, therefore, have to be finely tuned and managed.

Disruptions or miswiring between these areas has a profound impact on language-processing ability. In fact, in high functioning autism, basic information acquisition may be intact, but ability to process information and integrate are affected, whereas, in low functioning autism, there is poor development of functional connection between the sensory cortex and association cortex, which is essential for such integration of information and processing to take place. Such lower functional connectivity has been found in autism in brain regions concerned with language, social cognition, problem solving, and working memory.

In summary, **the difficulty that a person with developmentally disability experiences in regulating behaviours and emotions, in communicating, and in modulating sensory inputs, has a significant bearing on the person's ability to adapt and function.**

In this brief and simplified discussion, I have outlined the dysfunction in the frontal executive system, the disruptions in the connectivity within the brain and the developmental immaturities in the brain that eventually lead to maladaptive responses. Awareness of the underlying neurobiological mechanisms helps us design intervention programs that are more effective in helping many of these vulnerable individuals, and in improving the quality of their lives.

Recommended Reading List

Minshew, N.J., and Williams, D.L. *Cortex, connectivity and neuronal organization.* Archives of Neurology, 2007; 64(7)

Dapretto M., Davies M.S. and Pfeifer J.H. *Understanding emotions in others: mirror neuron dysfunction in children with autism spectrum disorder.* Nat Neurosci. 2006; 9(1)
Luna B et al. *Maturation of executive system in autism.* Biol Psychiatry. 2007; 61(4)

Julia P. Owen, Yi-Ou Li, Etay Ziv, Zoe Strominger, Jacquelyn Gold, Polina Bukhpun, Mari Wakahiro, Eric J. Friedman, Elliott H. Sherr, Pratik Mukherjee. The structural connectome of the human brain in agenesis of the corpus callosum**.** *NeuroImage*, 2013; 70: 340 DOI: 10.1016/j.neuroimage.2012.12.031

Jurriaan M Peters, Maxime Taquet, Clemente Vega, Shafali S Jeste, Ivan Sanchez Fernandez, Jacqueline Tan, Charles A Nelson, Mustafa Sahin, Simon K Warfield. Brain

functional networks in syndromic and non-syndromic autism: a graph theoretical study of EEG connectivity**.** *BMC Medicine*, 2013; 11 (1): 54 DOI: 10.1186/1741-7015-

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http://www.theglobeandmail.com/technology/science/brain/how-poverty-influences-a-childs-brain-development/article7882957/

How poverty influences a child's brain development

IVAN SEMENIUK, The Globe and Mail, Published Friday, Jan. 25 2013, 5:53 PM EST, Last updated Friday, Feb. 01 2013, 7:03 PM EST

Folic Acid Linked to Lower Autism Risk

Association Between Maternal Use of Folic Acid Supplements and Risk of Autism Spectrum Disorders in Children

Pål Surén, MD, MPH; Christine Roth, MSc; Michaeline Bresnahan, PhD; Margaretha Haugen, PhD; Mady Hornig, MD; Deborah Hirtz, MD; Kari Kveim Lie, MD; W. Ian Lipkin, MD; Per Magnus, MD, PhD; Ted Reichborn-Kjennerud, MD, PhD; Synnve Schjølberg, MSc; George Davey Smith, MD, DSc; Anne-Siri Øyen, PhD; Ezra Susser, MD, DrPH; Camilla Stoltenberg, MD, PhD

A study of 85,176 Norwegian children finds that women who took folic acid supplements beginning a month before conception through eight weeks into pregnancy had a 40 percent lower risk of giving birth to children with autism.

JAMA. 2013;309(6):570-577. doi:10.1001/jama.2012.155925

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http://www.microbecolhealthdis.net/index.php/mehd/article/view/19260

Microbial Ecology in Health and Disease Vol 23(2012)

Short-chain fatty acid fermentation products of the gut microbiome: implications in autism spectrum disorders

Derrick F. MacFabe

See also in the same issue: **Thematic cluster: Focus on autism spectrum disorders** http://www.microbecolhealthdis.net/index.php/mehd/issue/view/1430

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http://www.psychiatry.org/dsm5

On this page you will find articles, fact sheets, and videos that explain the new organization and features of the DSM-5, the diagnostic differences between DSM-IV-TR and DSM-5, and the development process behind the new edition.

DSM-5 Provides New Take on Neurodevelopment Disorders

Mark Moran: "The chapter on neurodevelopmental disorders comes first in *DSM-5*'s diagnostic section, reflecting a lifespan approach to the manual's organization." ***Additional information, including video interviews with Susan Swedo, M.D., on ASD and specific learning disorder, and with David Kupfer, M.D., and Dilip Jeste, M.D., on the development of DSM-5, is posted at http://www.psychiatry.org/dsm5***

See also http://psychnews.psychiatryonline.org/newsarticle.aspx?articleid=1558424

Journal of Intellectual Disability Research, March 2013 Vol 57(3), Pages 201-292

Factors associated with hospitalisations for ambulatory care-sensitive conditions among persons with an intellectual disability – a publicly insured population perspective (pages 226–239) Article first published online: 28 FEB 2012 | DOI: 10.1111/j.1365-2788.2011.01528.x

R. S. Balogh, H. Ouellette-Kuntz, M. Brownell and A. Colantonio

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http://www.nature.com/tp/journal/v3/n1/abs/tp2012143a.html

Original Article

Citation: *Translational Psychiatry* (2013) **3**, e220; doi:10.1038/tp.2012.143
Published online 22 January 2013

Unique acyl-carnitine profiles are potential biomarkers for acquired mitochondrial disease in autism spectrum disorder

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