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Beyond the Three Dimensional Aspects of Neuro-anatomy: The Multidimensional Brain

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In addition to the three dimensional components characteristically associated with macro anatomy, the brain is an organ that changes with time and experience, has fast and slow neurotransmission (time), is able to change itself genetically as well as switching genes on an off and so adjust its epigenetic component that can cross generations. In addition we have a Wi-Fi like mirror neuron system network that allows communications with others not only through language but emotional and social cue interpretation what has been called theory of mind.Not only do we have our own intranet but are also connected globally with other brains that influence us – an internet in other words. Visible macroanatomic changes may variously reflect the underlying, at times extensive microscopic changes.

The critical importance of neuro-anatomy has been elegantly demonstrated in the neuroarcheological discipline and provided us with inferences about the study of language origins, termed the "big bang theory of human evolution". Bipedalism, led to tool making, a tripling in brain growth, the development of increasing fronto-parietal networks, culminating in the mirror neuron networks, the latter which is now providing hypotheses of some very common, challenging and ill understood syndromes, such as attention deficit hyperactivity disorder and autism. Although we are used to macroscopic neuroanatomical images being static over time, it is important to recall that the brain is the most metabolically active organ in the body and has marked plasticity potentialthat pertains to both gray and white matter. Although the changes are mostly synaptic, neuronal network and at a cellular level, gross anatomical brain changes are visible as for example in autism. For example there is a paucity of glial cells in the frontal networks in schizophrenia and an excess in certain epileptic syndromes. Albert Einstein's left inferior parietal lobe had approximately twice the number of glial cells compared to age and gender matched controls. Such anatomical changes underlie the powerful abstraction and creativity ability that gave us the theory of relativity for example.

Macroscopic anatomy is traditionally defined as body structures that are visible to the naked eye. Brodmann and Golgi were both major contributors to our understanding of the gross anatomical complexity and making sense for us of the multitude of anatomical regions. Since then several atlases of gross anatomy have been published each with differing emphasis. At least six differentcytoarchitectonic brain atlases reflect the challenge of the gross and microanatomical aspects alone [1]. A recent refinement is the probabilistic human cortical mapping pioneered by the Jülich – Düsseldorfcytoarchitectonic atlas [2]. The influx of physiological data from functional imaging such as functional MRI and PET scanners have started to yield ancillary approaches as well as receptor imaging maps [3]. This multi-dimensional aspect of cerebral neuro-anatomy in terms of not only gross anatomical gyral, subcortical components for example, but also the fiber tracts, histological aspects and activation patterns give credence to the supposition of multidimensional components of neuro-anatomy.

The burgeoning multidisciplinary data is blurring the neuro-anatomical boundaries. For example the radial glia guiding the 100 billion neurons and up to 100 000 synapses per neuron in human development yielding approximately 10 quadrillion synapses (or 10^{16}), an unimaginable number for us to comprehend. More recently it has become appreciated that glial cells outnumber neurons 6:1 and a fourth type of glial cell, NG2 cells, may represent a kind of sleeper cell that is capable of transforming into not only new other glial cells, but neurons. This dynamic nature of the brain and its remodeling capability have only recently been appreciated. Furthermore, the brain changes itself through experience, activities and medications. Experience dependent (juggling) causes changes in white matter microstructure and growth [4].

Less is sometimes more. Spindle cells appear postnatally, appear only in hominids, cetaceans and not in pongids, localized in the anterior cingulate, fronto insular and prefrontal cortex and connect with diverse parts of the human brain. They are regarded as a key feature of intelligent behavior, adaptive behavior and cognitive dissonance, the motivation to act and regulate our emotions and the hallmarks of humanness. They are also implicated in disease states such as autism and Alzheimer's disease. Lesions of these neuroanatomical sites, Brodmann Area (BA) 24, BA 10 for example, may be inconspicuous to the casual clinician but have enduring consequences on behavior. Understanding neuro-anatomy and its ramifications are therefore key in interpreting clinical conditions.

Multimodality MRI has enabled imaging not only of fine anatomical detail and vasculature (for example 7 tesla scan of middle cerebral artery perforators) [5], but also fiber tracts of the brain by diffusion tensor imaging (DTI). Students of the clinical brain sciences now are able to consult not only neuro-anatomy texts but complement the analysis of brain scans with multicolored (for dicephering 3 dimensional direction) fiber tracts of the brain that are important for many clinical entities but most importantly traumatic brain injury, stroke and multiple sclerosis [6].

Functional imaging (f-MRI, PET, SPECT) has made impressive strides. Long before cerebral atrophy becomes visible on anatomical scans, PET brain imaging may detect the earliest signs of hypofunction in Alzheimer's disease, frontotemporal lobe disorders, diffuse Lewy body disease and posterior cortical atrophy syndrome, for example. The idling human brain or resting state networks or the default mode

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network (DMN) by f-MRI, at first a curiosity is becoming potentially the most important imaging procedure for neurodegenerative diseases. Large-scale brain networks depicted by DMN include the salience and attentional networks as well as those pertaining to language, emotional processing, memory, vision and movement [7,8].

The imaging role in lesion localization is now depicted by the two big imaging domains, anatomical and functional which are complementary in nature. At times it is important to interpret anatomical lesions in the context of remote effects of a lesion (diaschisis). A relatively novel clinical approach of lesion localization, in terms of hypo and hyperfunction and hodological hypo and hyper connection is based directly on gross neuroanatomical gyral and subcortical structure and fiber tract anatomy [9]. Clinical examples include frontal network syndrome such as imitation behavior and the brain's visual system, another widely ramifying system, this time of the posterior cortex and its conundrum of visual disorders. This approach facilitates thepathophysiological understanding. Changes in anatomy also occur in a deleterious way such as that seen by DTI and fractional anisotropy (FA) in smokers. Importantly it can be shown that within 10-20 years after smoking changes, these white matter changes improve, as does cognitive functioning [10].

Maintaining a multidisciplinary perspective is becoming increasingly relevant to the study if neuro-anatomy as it isindeed important to all medical disciplines. At the same time appreciating the pivotal role of gross anatomy in initial localization is akin to an Inuksuit in guiding humans in a much earlier phase of our development.

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