

# Connectivity Matrices and Correlations of Corpus Callosum Thickness as an Approach to Evaluating Neuroanatomical Correlates of Cognition

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#### Abstract

Connectome matrices are increasingly instructive in the evaluation of human brain neuroanatomy. Data collected for the human brain connectome reveals elaborate intricacies of the human brain and what makes us unique and diverse. White matter density differences, for instance, can be correlated with quantity of information flowing through a particular brain region, which, in turn, may suggest potential neuroanatomical correlations with cognitive ability.

Keywords: Corpus callosum; Neuroanatomy; Cognition

## Introduction

Connectome matrices are increasingly instructive in the evaluation of human brain neuroanatomy. Data collected for the human brain connectome reveals elaborate intricacies of the human brain and what makes us unique and diverse. White matter density differences, for instance, can be correlated with quantity of information flowing through a particular brain region, which, in turn, may suggest potential neuroanatomical correlations with cognitive ability.

The corpus callosum (CC) is the largest single white matter structure in the brain and directly or indirectly regulates many processes such as language, visuo-spatial appreciation, and motor control, to name a few. Anatomical variance between individuals can be great in any given region, presumably altering the cognitive processes for which it is responsible. For example, gross anatomical studies of Albert Einstein's brain have revealed various differences compared to control brains [1,2]. The thicker CC measurements indicate increased fiber density and subsequently greater potential for activity and function. We will contrast connectivity matrix images that demonstrate normal CC white matter density distribution with known CC thickness variations in the brain of Albert Einstein as determined by gross and histologic inspection.

#### **Connectome technology**

The Human Connectome Project, with support from the National Institutes of Health (NIH) and other NIH institutes, is leading the way in human connectomics. Information is collected and processed at various partnered institutions such as the University of Southern California (USC)-Massachusetts General Hospital (MGH) and the Laboratory of Neuro Imaging, Martinos Center at Massachusetts General Hospital; and Washington University-University of Minnesota and Human Connectome.org, Van Essen Lab, Center for Magnetic Resonance Research. The Human Connectome Project (HCP) has assembled a structural and functional map of human neural connections in vivo within and across individuals (http:// www.humanconnectomeproject.org/about/) [3].

October 6, 2011 marked the first time that human diffusion scans had been obtained from the 3.0 Tesla Seimens Connectome scanner at the MGH-USC Human Connectome Project (HCP). The scanner was programed to execute a set of customized imaging sequences, incompatible to runs on non-connectome platforms. Soon after, HCP began hosting brain-mapping seminars to explore methods in neuroscience useful for biomarker discovery in neuropathologic disease processes.

# The Role of Callosal White Matter Thickness Correlations for Inferring Connectivity

The corpus callosum, sometimes referred to as the great cerebral commissure, contains the largest bundle of fibers that connect the two cerebral hemispheres and is a valid point of reference for study of thickness correlations. Thickness relates to increased fiber number and greater inter-hemispheric connectivity [4] and is suggested in the involvement of any neuroanatomical substrate of hemisphere specialization [5]. Einstein's corpus callosum was found to be thicker in comparison to male control brains in his age range measured at 400 points, and mostly thicker even compared to younger controls (Figures 1 and 2) [1].

Callosal tracts are organized topographically [5-7]. The dorsal CC region receives fibers from the medial and dorsal cortical lobes. Similarly, the ventral CC region receives connections originating from the lateral cortical lobes. Einstein's entire callosum was thicker than the older controls, and interestingly his callosal genu, midbody, isthmus and part of the splenium are thicker except in the most rostral body, compared to the younger controls. Luders et al. [8] found callosal morphology correlates thickness with intelligence measures and, "positive associations between intelligence and posterior callosal thickness may reflect a more efficient inter-hemispheric information transfer, positively affecting information processing and integration, and thus intellectual performance."



Figure 1: Photographs of Einstein's medial brain showing the corpus callosum (Falk et al.)[2].



**Figure 2:** Graph showing Einstein's (red line) thickness is more than the older controls (blue line) at every point, and thicker than the younger controls (green line) in the majority of points. "The selected and registered average corpus callosum thickness plots, Einstein (red), the elderly control (blue) and the young control group (green); labels after Witelson [5]. Purple (old controls) and cyan (young controls) spans indicate that these regions differ significantly (P<0.05, FDR corrected) between Einstein and the two age control groups. Red arrows indicate that Einstein's callosal thickness is 10% thicker than the mean for the younger group, especially in the splenium, whereas the width of Einstein's corpus callosum is noticeably larger in the genu" [1].

# Corpus Callosum (CC) Anatomy and Function

# CC rostrum and genu fibers

These fibers connect inter-hemispheric regions of orbital gyri, ventral and dorsal prefrontal cortices that correspond to bilateral Brodmann areas (BA) 11/10, and help to plan, reason, make decisions, retrieve memories, and perform executive function [6,9,10]. Greater callosal thickness in the rostral and genu regions of Einstein's brain [1] is consistent with larger prefrontal cortices, an extraordinary prefrontal cortex, and inferior portions of the primary somatosensory

and motor cortices greatly expanded in the left hemisphere [2]. This "may have provided underpinnings for his exce8ptional cognitive abilities and remarkable thought experiments" [1]. This is consistent with the statement by Aboitiz et al. [4] that these fibers are indeed involved in the transfer of cognitive information (Figures 3 and 4).

# CC midbody and isthmus

These fibers are able to transmit information faster than others because of the larger size in heavier myelination [4]. They connect the premotor cortices (BA 6), primary motor cortices (BA 4), primary somatosensory cortices (BA 1/2/3), secondary somatosensory cortices (BA 5), and parts of the parietal region [9,10] all involved with perception, spatial awareness and sensory-motor functions. Einstein's CC midbody and isthmus were thicker than controls [1].



**Figure 3:** Corpus callosum fibers as shown on the human connectome. View is of right inferior corpus callosum, anterior is to the right of photo. The fibers are color-coded by direction: red=left-right, green=anterior-posterior, blue=up-down.

# CC isthmus

This region connects sensory-motor cortices [9]; primary sensory (even primary motor), posterior parietal, and (superior) temporal

cortices [8]. A "knob" noted in the right primary motor cortex, perhaps explained by his right-handed violin playing since childhood, relates to a corresponding callosal thickness in the controls [1].



**Figure 4:** Corpus callosum fibers as shown on the human connectome. View is of right corpus callosum, anterior is to the right of photo. The fibers are color-coded by direction: red=left-right, green=anterior-posterior, blue = up-down. Credit: Courtesy of the Laboratory of Neuro Imaging and Martinos Center for Biomedical Imaging, Consortium of the Human Connectome Project http://www.humanconnectomeproject.org [2].

## CC posterior isthmus and splenium

Connects superior parietal lobules (BA 7), inferior parietal lobules (BA 39/40), and temporal cortices (BA 20/21/37). The parietal lobes contribute to verbal, spatial, and number related processes while the temporal lobes are involved with processing sound and sensory input, language comprehension, visual memories and the retention of new memories, meaning, and emotion. Specifically high-level visual processing, recognition memory face and body recognition, and color processing involve the inferior temporal gyri (BA 20) [11].

#### CC splenium

This area connects the superior parietal lobules, inferior parietal lobules, temporal cortices as noted above, and occipital cortices (BA 17/18/19) [8-10]. Einstein's splenium was thicker than controls [1]. The splenium also transfers cognitive information between the hemispheres and facilitates higher-order processing [4]. Of interest, spatial attention and imagery processes are focused in the superior parietal lobules along with visuomotor coordination [12], and are activated with mental arithmetic and digit memory tasks shown on functional MRI studies [13,14]. Inferior parietal lobules help to integrate visuomotor processes, in addition to coordinating language, mathematical operation (especially on the left), and spatial perception [15]. Occipital cortices manage visual processing and O'Craven and Kanwisher [16] found they could be activated doing imagery with the eyes closed (2000). Relatedly, Einstein's Autobiographical Notes [17,18] details his thought experiments that he often performed while daydreaming. One such daydream, chasing a beam of light as it travelled through space, was the germ for his special theory of relativity.

# **Future Clinical Applications**

Thus far, connectome technology is embryonic regarding the ability to infer neuroanatomical-cognition correlates. However, we anticipate the ongoing research of healthy brains will contribute to the existing known correlates from post-mortem studies and technologies such as fMRI and form a foundation of comparison to neuropathology. The technology has great potential as a clinically meaningful tool for biomarker identification. One such application would be the use of matrices to analyze posttraumatic encephalitic brains of the estimated 1.6 to 3.8 million players diagnosed with sports-related concussions/ mild traumatic brain injuries per year (Centers for Disease Control and Prevention, 2014) [19].

Connectome matrices might also yield long sought Alzheimer's Disease biomarkers. According to Brown [20], "Alzheimer's Disease (AD) accounts for more dementia diagnoses than all other causes combined in the United States. More common in women than men, after 65 years of age, AD is the fifth-leading cause of death and remarkably, the percentage of people afflicted doubles in every subsequent five-year age group, resulting in a prevalence as high as 50% for persons 95 year of age and older. The brain plaque suggestive of AD appears long before the signs and symptoms, leaving wide open the possibilities for delay, as well as treatment and possibly curing this disease."

Therefore, any plaque-specific imaging modalities that may emerge from connectome technology would go a long way towards the preclinical detection of AD.

Rheumatoid arthritis and fibromyalgia are two more examples of how the diagnostic ability of connectome technology might be exploited. The technology has evolved enough to differentiate, albeit ambiguously, between the default networks of controls and afflicted subjects [21].

Data of healthy brains is being collected and made readily available in a connectome as a "neuroinformatics resource that could be used in virtually all areas of experimental and theoretical neuroscience" [22]. "Future studies of the human connectome will greatly expand our knowledge of network topology and dynamics in the healthy, developing, aging, and diseased brain." [23]. We may be able to explore potential neurobehavioral relationships between these neuroanomalies in the context of the data extracted from connectome matrices.

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