RELATIVE PREFRONTAL CORTEX SURFACE AREA IN *PAN TROGLODYTES* AND *HOMO SAPIENS* AND ITS IMPLICATIONS FOR COGNITIVE EVOLUTION

by

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ABSTRACT

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The human prefrontal cortex (PFC) is associated with complex cognitive behaviors such as planning for the future, memory for serial order, social information processing, and language. Understanding how the PFC has changed through time is central to the study of human neural evolution. Here we investigate expansion of the PFC by measuring relative surface area of the PFC in *Pan troglodytes* and *Homo sapiens*. Magnetic resonance images (MRI's) from 8 preserved chimpanzee brains (3 male and 5 female adults) were segmented and measured. The results of this study indicate that there are gross anatomical differences between the chimpanzee and human prefrontal cortex beyond absolute size. The lower surface area to volume ratio in PFC of the chimpanzee when compared to a human indicates less gyral white matter in this region and thus, less associative connectivity. This anatomical evidence of a difference corresponds with the lesser cognitive complexity observed in chimpanzees.

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List of Tables x

List of Figures xi

CHAPTER 1: Introduction 1

CHAPTER 2: Background 3

2.1 Introduction 3

2.2 Brain Size 3

2.3 Frontal Lobe 5

2.4 Tissue Proportions 7

2.5 Prefrontal Cortex 7

CHAPTER 3: Materials and Methods 13

3.1 Introduction 13

3.2 MRIs 14

3.3 Segmentation 15

3.4 Prefrontal Cortex Boundaries 18

3.5 Reliability 19

3.6 Thesis Statement 21

CHAPTER 4: Results 23

CHAPTER 5: Discussion 27

5.1 Introduction 27

5.2 Theoretical Considerations: Significance of Surface Area to Volume Ratios 27

5.3 Implications of Research 31

References Cited 33

LIST OF TABLES

Table 1: Descriptive data on chimpanzee brains 13

Table 2: Reliability assessment 20

Table 3: Raw results 25

Table 4: Measurement results 26

Table 5: Test data on a cube and a sphere of increasing size 29

LIST OF FIGURES

Figure 1: Volume of frontal cortex of various apes 6

Figure 2: Prefrontal cortex in humans and apes 8

Figure 3: Prefrontal cortex in baboon and human brains 10

Figure 4: Relative size of the prefrontal in primate 11

Figure 5: 3D models generated after MRI segmentation 16

Figure 6: 3D Properties module in Mimics v.11.1 17

Figure 7: Chimpanzee brain "Dath" with PFC highlighted 19

Figure 8: Examples of test shapes. 28

CHAPTER 1: Introduction

The task of understanding the evolution of the human brain will likely not be solved entirely by studies of the fossil records. The field of comparative neuroanatomy among human's closest living ancestors (i.e., extant primates) is one way to look at structures that have been conserved and those that have changed throughout evolution. In particular, focusing on areas responsible for particular behaviors (or limited sets of behavior) across species has produced important breakthrough in our understanding of brain evolution. The human prefrontal cortex (PFC) has been described as "a crowning achievement of the human brain… that, like the rest of the brain, is a work in progress" (Grafman, 2002). The PFC has been intimately associated with behaviors that are used as measures of cognitive ability such as planning for the future, memory for serial order, and social information processing (Damasio, 1985; de Bruin et al., 1990; Fruster, 1985). Compared to great apes and other primates, the human PFC has unequally expanded throughout evolution to accommodate the increased behavioral complexity that is controlled by this region of the cerebrum (Schoenemann et al., 2005).

With the absence of neural tissue in the fossil record, extant primates are relied upon for comparison to modern humans. However, as noted by Sherwood et al. (2008), "…all living species are the product of their own evolutionary trajectory and cannot be stand-ins for fossil ancestors." Keeping this in mind, through comparison of differences between the human brain and homologous areas in brains of other nonhuman primates,

a greater understanding of human cognitive evolution can be realized. For this reason, the present study will investigate whether the relative surface area of the prefrontal cortex (i.e., the ratio of the surface area of PFC to overall cerebrum) differs in chimpanzees (*Pan troglodytes*) and humans (*Homo sapiens*). Clearly, the weight of the adult human brain is almost 3-times larger than that of chimpanzees (Rilling et al., 1999). Thus, the present hypothesis on potential interspecies difference will be conducted using comparative values of the surface area and volume of PFC relative to the total in the same species. In this way, and in spite of the great size differences, it should be possible to draw conclusions about the size of the prefrontal cortex in relation to the distinctly different behavioral differences (e.g., cognitive, serial order and social information processing) that distinguished humans from chimpanzees.

CHAPTER 2: Background

2.1 Introduction

One of the first steps in investigating evolutionary changes is to correct and control for differences in gross anatomical size and shape across species. The brains of human and nonhuman primates vary greatly in size and shape. For example, the brain the new world marmoset monkey weighs only about 7 g and is no larger than a few cm^3 compared to the adult human brain that weighs 1350 g on average and is 1100 cm^3. The chimpanzee brain is closer to that of humans, but is still 3-times lighter (ca. 400 g) and almost 4-times smaller in volume (262 cm^3). Beyond absolute differences in size, there are major differences in connectivity and complexity in behaviorally repertoire that exists across species. While histological evidence would provide the best evaluation of complexity, sources of data (i.e. chimpanzee brains) are relatively scarce and thus invasive investigation is of their structure is beyond the focus of this study. Surface area of a region, in this case the prefrontal cortex, will be used as an evaluation of both complexity of the cortex as well as an indicator of the underlying connectivity.

2.2 Brain Size

In general, increases in total brain size in mammals are associated with increases in body mass. The largest absolute brain size in all animals is found in the largest

mammals such as elephants and whales (Nowak, 1999). In primates larger bodies, such as great apes and humans, develop brains that are absolutely larger than those of smaller primates such as lemurs and tarsiers (Stephan, 1969; Nowak, 1999). With respect to total brain size relative to body size, the trend is the opposite with brains becoming a smaller portion of the total mass of an animal. The expected mass of the brain for a given body mass is defined by the equation $E_{brain} = 0.12M_{body}^{2/3}$ (Jerison, 1973). While this formula predicts the brain mass from body mass for most vertebrates, some have larger brains then body size would predict. This deviation of measured brain mass (M) from expected brain mass (E) is referred to as an encephalization quotient (EQ) and is calculated from the equation $EQ = M_{brain}/E_{brain}$ (Jerison, 1973).

Humans outpace all other animals based on their diversion from the expected brain mass for a primate of human body size (Holloway, et al., 1982). The slope of the regression line of allometric scaling of brain mass vs. body mass is currently measured as 0.66 for most mammals (Macphail, 1982) and 0.76 for primates (Sherwood, et al., 2008). An EQ value above 1 is generally interpreted as a given species having "excess" brain tissue which is used for controlling abilities beyond somatic control of a large body. These extra functions, no matter how basic, are interpreted as being related to "cognition" (MacLeod, 2004). Previous studies show that humans have brains that are unusually large for a mammal of our body size, around 3 times larger than expected (Martin & Harvey 1985, Deacon 1997) The encephalization quotient for humans varies from ~5.3 all the way to ~8.1 depending on which adjusted formula a particular author uses (Jerison et al., 1973, Martin 1984). Despite this variance, human EQ is the highest compared to all other species. Human cognitive ability and intelligence is attributed to

this excessively large brain which, relative to other regions of the human body, has expanded and differentiated the most during human evolution (Holloway 1995).

Why is it then that all primates do not share a degree of human intelligence equal to their relative EQ? The various ways in which the human brain differs from nonhuman primates and what forces have driven these changes are perhaps the most interesting questions in the study of cognitive evolution. The divergence from primates during the evolution of the human brain can be found not only in the relative size of the whole brain, but also the unequal increases in the size of the different components. It is implicitly assumed that more tissue equals greater processing ability (Schoenemann 1997), and that humans should have larger brain components dedicated to particular behaviors such as complex social systems and foresight to plan for future events. In contrast, the human olfactory bulb, which is approximately 30% smaller than scaling would predict for a primate brain of human size (Stephan et al. 1981), is an example of a brain component that has been deemphasized during human evolution.

2.3 Frontal Lobe

The frontal lobe in particular is an area of interest because it has been agreed that it is larger in modern humans and that it is related to planning and higher-order thought. The frontal lobe is also easy to delineate across primate species as it includes all cortical areas anterior to the central sulcus. Previous studies have shown that the frontal lobe is the same proportionate size in both humans and the great apes (Semendeferi et al. 2002, Bush et al. 2004). The average human frontal cortex accounts

for approximately 37.7% of total brain volume, the same proportion that the frontal lobe takes up in other great apes (see fig.1 from Semendeferi et al. 2002).

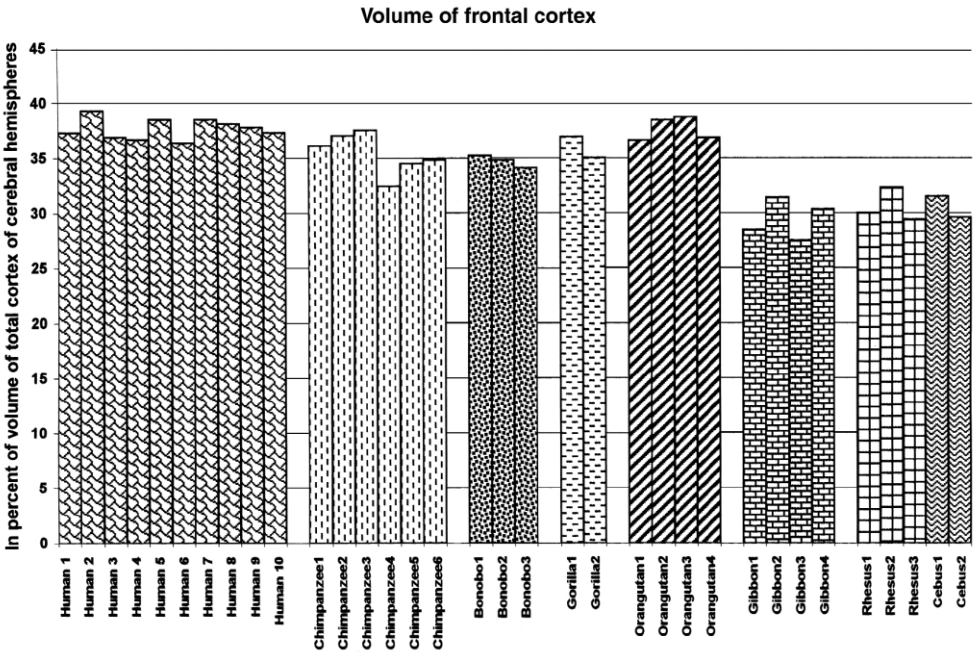

Figure 1: Volume of frontal cortex in humans and non-human primates (Semendeferi et al. 2002)

The frontal lobe contains three important functional divisions 1) the primary motor area related to conscious movement, 2) the premotor areas responsible for planning of complex movement, e.g., saccades and visual target acquisition, and 3) the prefrontal cortex that controls behaviors such as planning, social interaction, and language. When the individual areas of the frontal lobe are measured, it has been show that the primary motor and the premotor areas in human are only about 30% and 60%, respectively, of the values for great apes (Blinkov et al., 1968). One implication of this finding is that the regions for complex movement planning and especially conscious movement have not increased to the same extent as other areas of the human brain dedicated to higher-order cognition (Deacon 1997).

2.4 Tissue Proportions

Relative surface area is only one measure of cortical evolution. Another factor to consider is the proportion of grey to white matter. Neurons in the cortical grey matter project their axons via the underlying cortical white matter to convey sensory, motor and associative information to other neurons located throughout the CNS. A greater abundance of white matter is indicative of more connections, faster processing and greater overall integration of neural processing. Schenker et al. (2005) report that, relative to other apes, humans have more white matter near the surface of the cortex where gyral patterns are more complex. An increase in the volume of gyral white matter in certain regions of the brain is indicative of increased interconnections to neighboring regions (Fields et al., 2005). This greater white matter volume is further interpreted to indicate greater cognitive activity in that region (Schenker et al., 2005). Conversely, a loss of grey and white matter in certain disease states such as Alzheimer's disease; characteristically the cognitive impairment is Alzheimer's disease is correlated with decrease in cortical white matter, often termed "gyral atrophy"(Thompson et al., 2001).

2.5 Prefrontal Cortex

The prefrontal cortex is responsible for the coordination and modulation of purposeful behavior. At any given time the brain processes many sources of information, drawing from both current external stimuli and memories of past experience. The PFC governs which of these inputs receives the most attention, at which time they are processed, and which information is given less importance and is

even ignored completely. It is this ability of the PFC to direct information in the same way that a conductor would direct an orchestra that makes the PFC essential in molding behavior.

The PFC in humans is larger than expected for a great ape of comparable body size since the other regions filling the frontal lobe, the primary and premotor cortexes, are smaller than expected (Schoenemann 2006). Brodmann (1912) referred to the PFC as the "region frontalis" and described is size to be 29% of the cortex in humans, 17% in the chimpanzee, 11.5% in the gibbon and macaque, and 8.5% in the lemur. However, more recent comparative studies investigating the size of the PFC in humans and great apes have provided conflicting results and interpretations. One study found that area 10 of the PFC was larger in humans than in great apes with respect to both absolute and relative brain size (Figure 2).

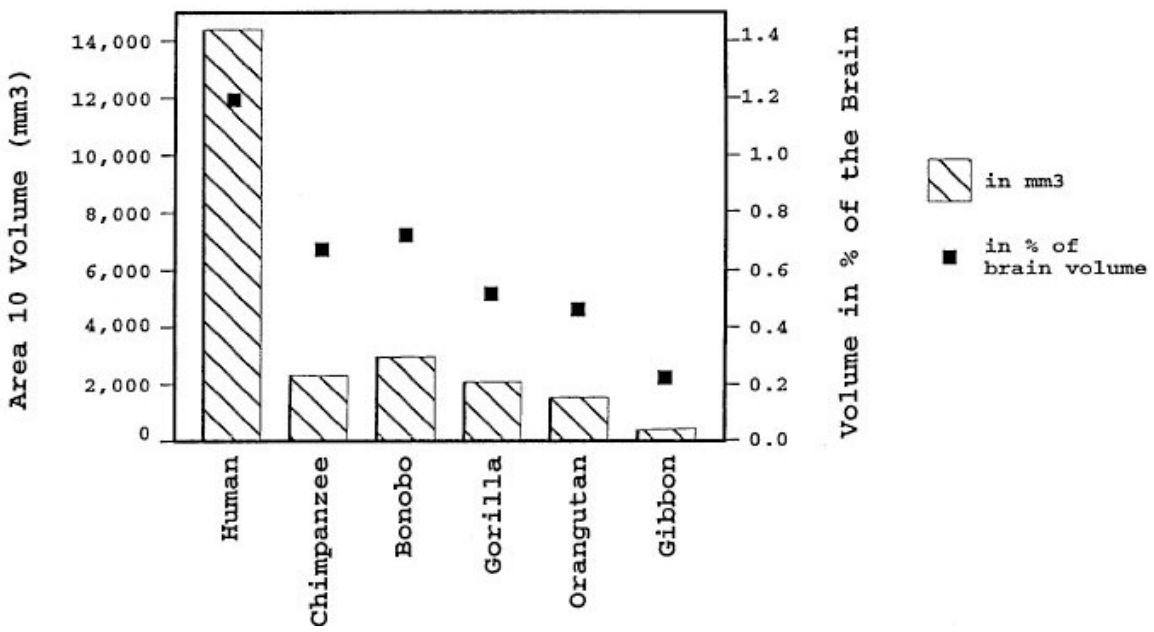

Figure 2: Prefrontal cortex in humans and apes (Semendeferi et al. 2001)

Rilling et al. (1999), in contrast found that the neocortex of extant primates were studied for the purpose of making inferences into how the brain has changed throughout evolution from the last common ancestor. The data showed that the hominid neocortex has expanded beyond allometric projections in gross size. The growth of grey matter and white matter was also found to be disproportionate with white matter in the PFC expanding faster than grey matter during human brain evolution. Rilling et al. (1999) also showed that the human PFC was significantly more convoluted as represented by gyrification index or GI than other nonhuman primates. The gyrification index measures cortical folding by comparing the length of the total neocortical surface to the length of the exposed surface cortex (Zilles et al., 1989). This measure of cortical convolution is easily implemented but has faced criticism over its precision and accuracy (Schaer et al., 2008). The significant difference was observed in the first slice of the MRI series that Rilling et al. (1999) used in their study which corresponded with a slice running through the PFC in all primates studied. This increased gyrification is indicative of increased function in the underlying cortex and possibly increased cognitive ability.

In contrast to the above studies, other analyses indicate that indicate that increases in the PFC are negligible, at best, and are not correlated with increases in function and complexity. In a study of the proportionate volume of the PFC in humans and baboons, McBride et al. (1999) found that the human PFC was significantly larger than that of a baboon. The actual difference was measured to be less than 2 percentage points. McBride et al. (1999) argued that such a modest increase in volume in the PFC

could not account for the vastly increased higher order cognitive function found in humans (Figure 3).

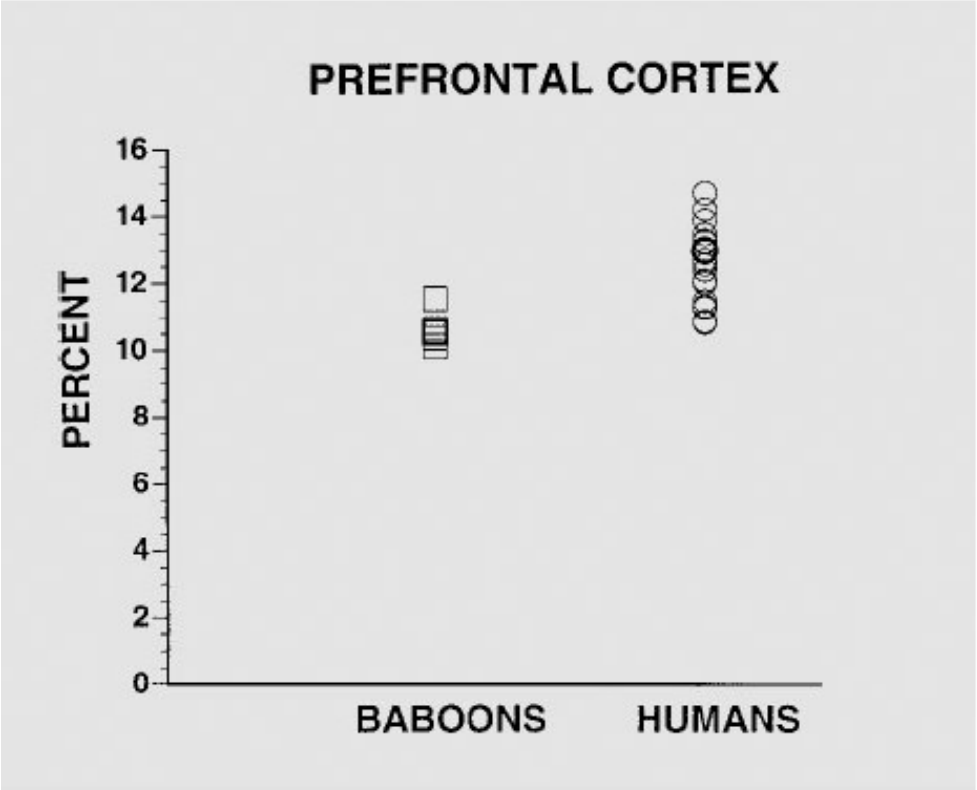

Figure 3: Proportionate volume of prefrontal cortex in baboon and human brains (McBride et al. 1999)

These noted differences between studies can be attributed to small sample sizes and methodological concerns about how to measure the prefrontal cortex. Using magnetic resonance images, MRI's to recreate and measure brains in a virtual environment has proved problematic and yielded conflicting results because no reliable sulcal boundaries exist for the PFC as do for other lobes of the brain. Schoenemann et al. (2005) along with other neuropsychological studies (Zipursky et al. 1992, Sax et al. 1999) have quantified the prefrontal cortex by including all tissue anterior to the genu of the corpus callosum. Although this method provides reliable operational boundaries of

the PFC, it does not define the prefrontal cortex cytoarchitecturally as originally proposed by Brodmann (1909, 1912) and the strict boundaries have the tendency to underestimate the size of the PFC across species. Schoenemann argued that magnitude of underestimation of the size of the PFC by this proxy method increases as the relative size of the PFC increases across the primate line. However, using this method the human brain is still significantly larger than expected for a nonhuman primate.

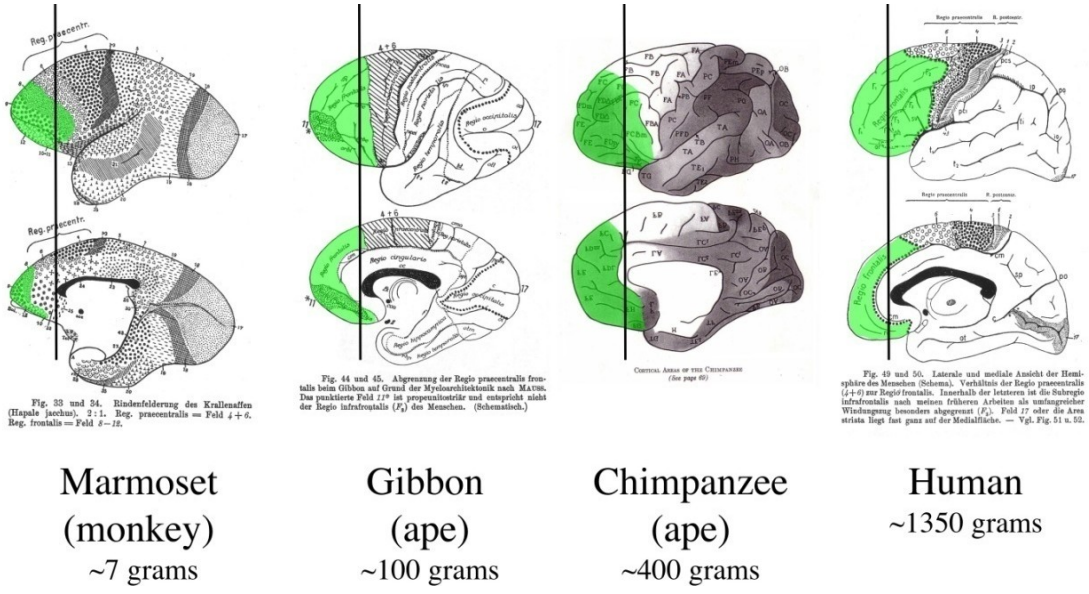

Figure 4: Relative size of the prefrontal in primate: cytoarchitecture vs. MRI proxy. Green area represents prefrontal defined cytoarchitecturally; vertical lines mark the most anterior point on the corpus callosum (MRI proxy demarcation uses all tissue anterior to this line); Marmoset, Gibbon, Human: Brodmann 1912; Chimpanzee: Bailey et al 1950 (Schoenemann et al. 2005)

In my thesis research I propose to further investigate the expansion in the PFC during human evolution. By measuring the relative surface area of the prefrontal cortex in *Pan troglodytes* and comparing it to previously published data from *Homo sapiens*, I hope to show that this area of the brain expanded through evolution to meet the increased functional complexity of human behavior. To help address some of the

conflicting findings by previous studies, I will utilize a larger sample size of chimpanzee brains (12 adults, 5 male and 7 female). To delineate the PFC, I will follow known boundaries in the chimpanzee brain. Where cytoarchitectural data is missing, I will use the plane through the genu of the corpus callosum as a posterior boundary. This is an intermediate method, half proxy, half anatomical boundaries. In addition to this method of delineation, I will also be measuring the surface area rather than the gross volume of all or part of the cortex. Surface area will give a better indication of complexity of this region beyond a two dimensional measure such as gyrification index. I will revisit the previous volumetric measurements of the PFC to both evaluate these findings and also to determine how my data varies based on this new measurement method.

CHAPTER 3: Materials and Methods

3.1 Introduction

I measured the surface area of the prefrontal cortex of *Pan troglodytes* based on virtual reconstructions of fixed brains and compared it to published values for *Homo sapiens*. I used Mimics v11.1 to construct models collect data in a virtual environment on brains reconstructed from structural MRI scans.

Table 1: Descriptive data on chimpanzee brains from which scans were taken.

Specimen ID	Name	Weight R (g)	Weight L (g)	Weight (g)	Sex	Slice Thickness	Screen Result
JH3	**	148.9	144.3	293.2	male	1.5 mm	Not Used
JH7	Tari	*	*	202	male	1.5 mm	Not Used
YN73074	**	154.9	153.0	307.9	female	1.5 mm	Not Used
YN77111	Frank	169.35	169.91	338.96	male	1.0 mm	Not Used
YN80	**	**	**	**	female	1.0 mm	Used
YN88256	Elena	157.9	157.4	315.35	female	1.5 mm	Used
YN92115	Chuck	181.18	183.62	364.8	male	1.0 mm	Not Used
YN92264	Cookie	**	**	**	female	1.0 mm	Not Used
YN94225	Francisca	*	*	400.5	female	1.0 mm	Used
YN95004	Sallie	*	*	361.6	female	1.0 mm	Used
YN95060	Halpha	185	200.3	385.3	female	1.5 mm	Used
YN95115	Robyne	*	*	300.7	female	1.0 mm	Used
YN97136	Keith	183.96	190.71	374.67	male	1.5 mm	Used
**	Dath	**	**	**	male	1.0 mm	Used

* denotes that the brain is whole and has not been separated into R and L hemispheres.
**data is missing or does not exist

3.2 MRIs

T1 weighted Magnetic Resonance Images of 14 individuals, 6 males and 8 females, acquired on a 1.5 Tesla GE Medical Systems Genesis Signa MRI scanner at 1.5 and 1.0 mm slice increments. These scans are from a collection of brains curated by Ralph Holloway and have been studied previously in several articles (Gannon et al., 1998, Sherwood et al., 2003, Holloway et al., 2003). This collection is currently curated in the Anthropology Department at Florida Atlantic University in Boca Raton, Florida. MRI scans were provided by Chet Sherwood performed at the Mount Sinai Medical Center in New York. Additional information about these chimpanzees can be found in Table 1.

After viewing the original 14 scans that were acquired, I determined that only 8 of them were complete and undamaged enough to give an accurate sample for this project. Deficiencies in the brains that were rejected for study included only half of the brain being represented in the scan (JH7, YN92115, and YN92264) and significant regions of the brain having been sampled for previous histological study (JH3, YN73074, and YN92264). The half brain scans can be doubled and the missing regions can be repaired in a future study but this would hurt the overall precision of the data. Reconstructions can deemphasize the sulcal depth that was actually present in the brain and mirroring left to right hemispheres masks possible contributions from asymmetry.

The MRI scans are in DICOM file format. I found it was important to use DICOM images because they would be free from processing errors that may result from being stacked in another program, such as ImageJ. Images previously converted into

.STL or ANALYZE formats can be problematic because of data loss, such as header data, during conversion.

3.3 Segmentation

MRI scans were imported into Materialize Mimics version 11.1 for segmenting and analysis. Segmentation is the process of dividing an image, in this case the slices of the MIRs, into different regions to define different structures. Mimics is a medical imaging software package that takes scanner data and converts it into CAD (computer-assisted design) compatible formats. Mimics has a robust segmentation suite that allows for a variety of different regions to be defined within a single MRI series. Different regions of interests are termed masks and can be overlaid upon each other and regions can be created with respect to previously created masks through cavity fill and region growing operations.

To create a mask, first a threshold tool is used to define a spectrum of grayscale that encompasses the structures of interest within the MRIs. Automated thresholding is a quick way to segment tissues of similar density. Tissue is selected based on a grayscale index relating to pixel color depth in the MR scans. While this alleviates much of the initial segmenting work, this automated process is not without drawbacks. Besides the inclusion of scan artifacts, the threshold tool will often obscure the true depth of a sulcus by extending the surface from one gyrus over a sulcus and onto adjacent gyrus. The resulting surface area measured on a mask generated from an automated threshold would be unpredictably less than the true surface area.

To correct for this error, after a mask has been generated from the automated threshold, I manually corrected the mask in areas where the surface is not accurately represented. This manual editing is also necessary to add or subtract artifacts that may be chosen because of gray level similarity rather than biological significance. The manual editing of the masks largely consisted on sulcus definition and deletion of non-brain matter that was present in the medium that the brains were suspended in during the scan.

Three-dimensional virtual models were generated from these masks after the initial editing on each two-dimensional slice. Further editing was performed as necessary after visualization of the 3D models. The models that were created for each subject were one for the whole cerebrum (total), one for the prefrontal cortex (prePF), and one for the area that was on the posterior of the PFC model (slice). This last model represents the surface area of the region were the PFC was "cut" away from the cerebrum and was excluded from measurement.

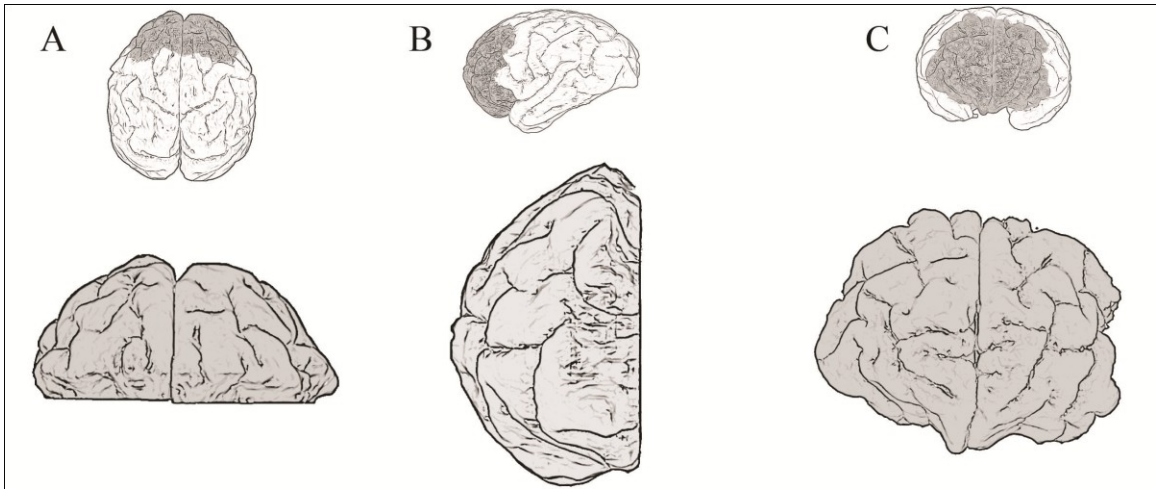

Figure 5: 3D models generated after MRI segmentation

Mimics has a measuring module (fig. 5) that allows descriptive measurements to be taken in two- or three-dimensional space. The "3d Properties" tool was used to give information about individual models (Table 3). This information includes linear measurements of size in the X, Y, and Z axes in mm, volume of the 3-D model in mm^3, surface area in mm^2, and number of triangles and points that are used in creation of the 3d mesh.

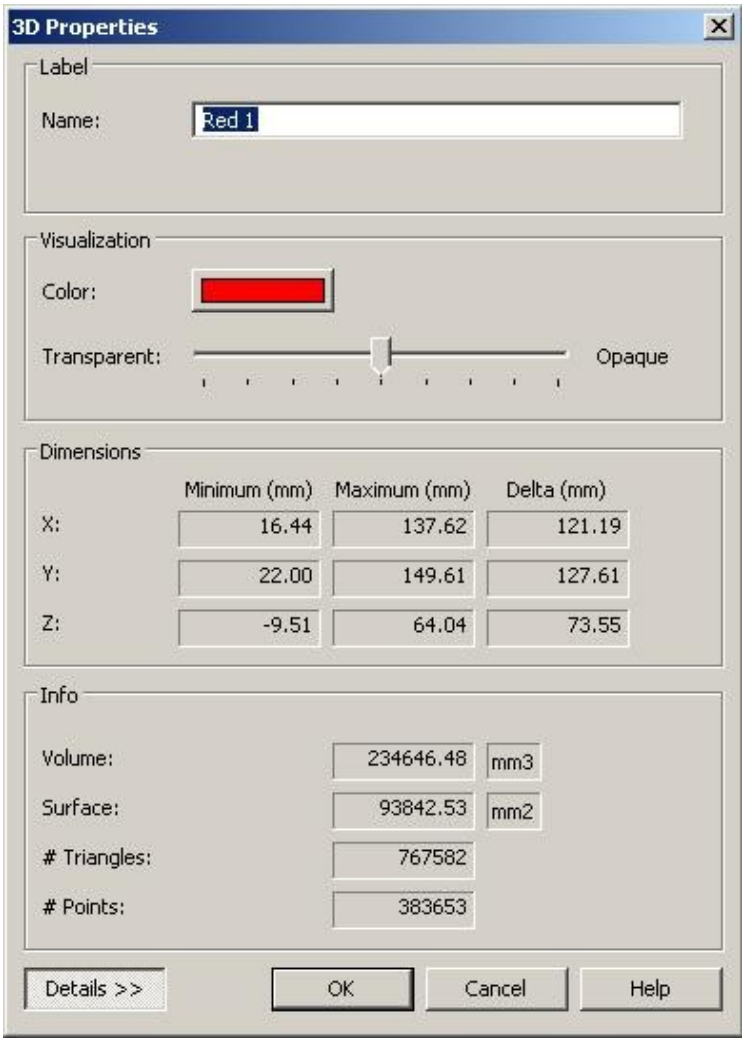

Figure 6: 3D Properties module in Mimics v.11.1.

3.4 Prefrontal Cortex Boundaries

The boundaries of the prefrontal cortex, specifically the posterior extent, are currently not well described for any primate species (Sherwood et al., 2005). Correlation between surface anatomical boundaries and cytoarchitectural boundaries is currently unreliable and not yet found to be uniform across individuals (Sherwood, Subiaul, & Zawidzki, 2008). Based on examination of examinations of cytoarchitecture maps (Brodmann, 1909, Economo et al., 1925, Sarkisov, 1955) and more recent interpretations (Hof et al., 1995, Semendeferi et al., 2001, Ongur et al., 2003), I will set the boundaries of the PFC as shown figure 6. The posterior boundary between the premotor cortex and the PFC follows superiorly along the inferior precentral sulcus. At the junction with the inferior frontal sulcus, I continue superior-medially towards the interhemispheric fissure, just posterior to the superior and medial frontal gyri, approximately between BA8 and BA9.

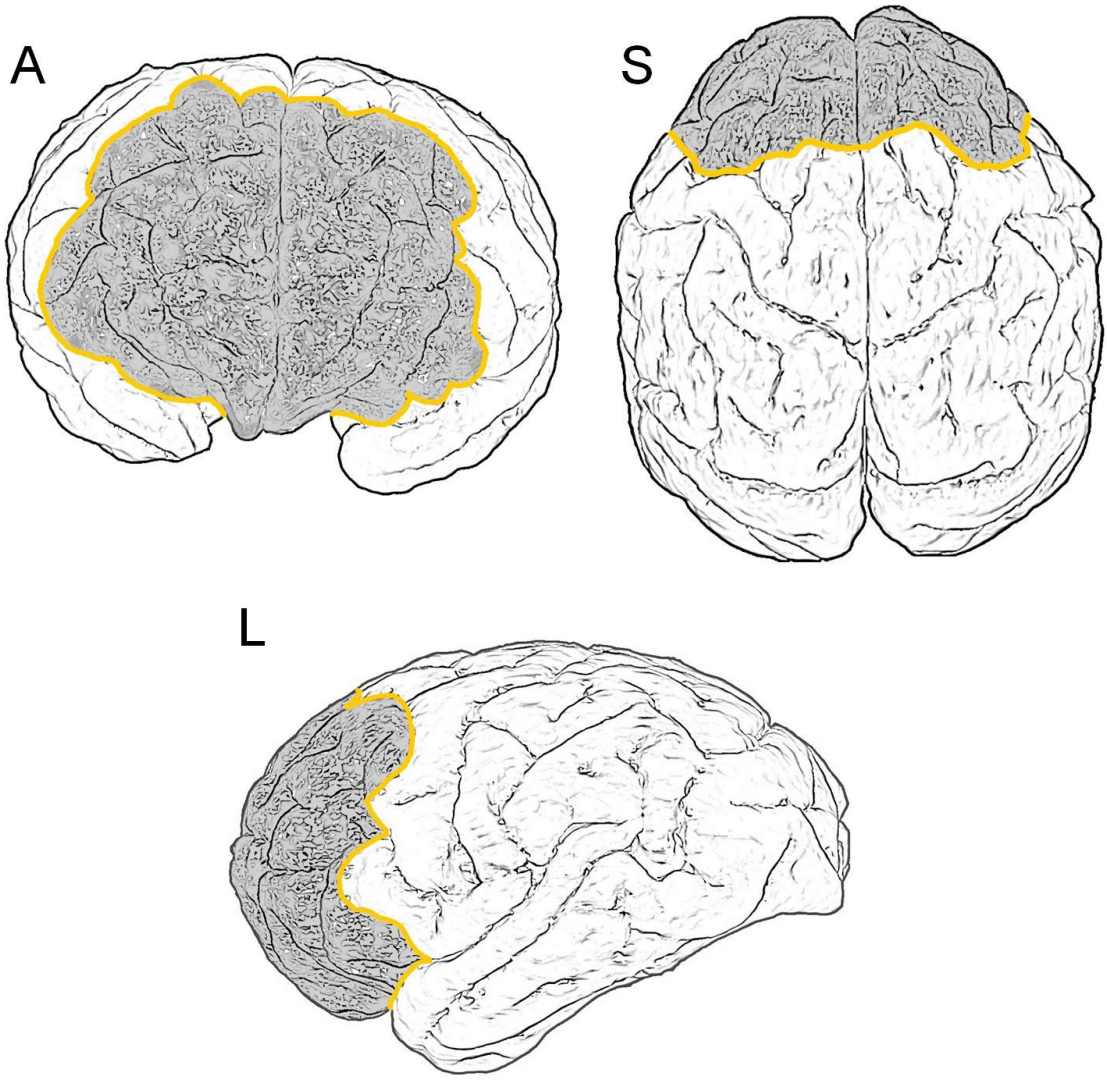

Figure 7: Chimpanzee brain "Dath" with PFC highlighted

3.5 Reliability

To measure test-retest error and reliability within this study I randomly chose 3 specimens and created 2 additional models of each of them. Repeated measures were obtained from three chimpanzee specimens (Dath, Elena, and Halpha) to generate multiple models for the same individual. With the time involved in manual

segmentation and PFC delineation, each reliability model 2 ("specimen_name"_rel2) were created at least a month after the original. The third reliability model ("specimen_name"_rel3) was created a week after the second model. Results from the reliability assessment are shown in Table 2.

Table 2: Reliability assessment.

	Dath		Elena		Halpha	
	Cerebrum	PFC	Cerebrum	PFC	Cerebrum	PFC
Model 1	520	137	528	128	566	129
Model 2	515	132	532	128	564	131
Model 3	517	139	533	129	560	126
Avg	517	136	531	128	563	128
Stdev	2.52	3.61	2.65	0.58	3.06	2.52
Error %	0.49	2.65	0.50	0.45	0.54	1.96

The multiple measures from each of the three experimental subjects differed by as little as 0.45-2.65% with Dath having the greatest error. This trial-to-trial error is relatively low give the possibility of experimental error in estimating the PFC boundaries that had to be redefined for each model and in each trial. In contrast, the cerebrum models overall had a much lower error, 0.49-0.54%, as the only potential error producing variable was sulcus definition. Based on these results, the model

making process used in this study is concluded to reliable and as was the method used to define the PFC posterior boundaries.

3.6 Thesis Statement

In this thesis I explore two hypotheses:

H_1: The relative surface area of the prefrontal cortex is larger in *Homo sapiens* than it is in *Pan troglodytes*.

H_0: The relative surface area of the prefrontal cortex is not significantly different in *Homo sapiens* and *Pan troglodytes*.

Secondly, relative surface area of the prefrontal cortices of chimps collected in this study will be compared to data from previous studies (Schoenemann et al., 2005) to determine if a "hybrid" method of measuring the PFC is more accurate.

H_2: Following known sulcal boundaries and delineating the PFC anterior to the GCC where cytoarchitecture is unclear will encompass all of the PFC.

H_0: Delineating the PFC by this method will not encompass a significantly different portion than proxy methods have.

By using the surface area of the PFC as a comparison, rather than the volume, better insight into the differences in size and complexity in the human and chimpanzee brain will be determined. Surface area is a better assessment of size in a region because

it considers gyral folding along with gross size in three dimensional spaces. Surface area will also give an indication of what volume of white matter in the PFC is located in the gyri. This white matter is especially important when looking at processing power and functional complexity in a region of the brain. White matter tends to have thicker myelin sheaths (Anderson et al., 1999) and neural conduction has been found to be faster in these wider, more myelinated axons (Jack et al., 1975, in Harrison et al., 2002). This faster neural conduction correlates with higher level of cognitive ability and thus gives an additional measure of expansion of neural tissue beyond size of the cortex and number of neurons present.

CHAPTER 4: Results

After measurement of the virtual models created in Mimics the data were exported for final analysis (Table 3). The slice value was halved and subtracted from the value for the prePF model to give the true surface area of the prefrontal cortex. This was necessary as the measurement tool did not distinguish which portions of the models were subcortical. Including the surface of the subcortical "slice" area would overestimate the surface area of the PFC. This correction was not necessary for volumetric measurements.

The surface area values for each of the specimens were averaged. As shown in Table 3, it was found that 23.37% of the surface area of the cerebrum in chimpanzee overlays the PFC. When compared to published human values (Tramo 1995, 1998; McBride 1999), the PFC surface area in humans is identical, i.e., it represents 23.14% of the total cerebrum surface area. As a percentage, the surface area of the PFC does not significantly differ between chimpanzee and human brains.

The surface area to volume ratio was next measured as it is more appropriate in the evaluation of biological shape. The surface area to volume ratio of the chimpanzee cerebrums within this study was found to be 2.18. The cerebrum in the human comparative data yielded a ratio of 1.73. These measures also do not significantly differ between chimpanzee and human. The prefrontal cortex surface area to volume ratio in the chimpanzee sample is 2.52. This is significantly different when compared to the

human ratio which is 3.21. Significance of all measured values was determined through a Kruskal-Wallis test, p value was set at ≤ 0.05. Full results can be found in Table 4.

Table 3: Raw results.

Name	**Total SA (mm2)**	**Slice SA (mm^2)**	**prePF SA (mm^2)**	**true PF SA (mm^2)**	**Total Vol (mm^3)**	**PF Vol (mm^3)**
Dath	52043.76	4464.36	15974.38	13742.20	249275.49	53170.38
Elena	52790.42	4293.06	14973.08	12826.55	233632.59	46472.53
Francisca	52110.70	5146.77	14826.12	12252.735	289727.67	56607.57
Halpha	56605.90	5644.01	15774.70	12952.69	301654.96	59410.52
Keith	66171.49	4639.34	14853.32	12533.65	283739.64	45693.44
Robyne	55290.41	5058.56	15215.89	12693.95	241231.70	47674.80
Sallie	67361.83	6886.79	20722.01	17278.615	278677.10	69827.08
YN80	50466.11	5177.56	13645.87	11057.09	203770.31	40349.04

SA is surface area, Vol is volume. "Total" is the whole cerebrum models; "Slice" is the model of the posterior, subcortical portion of the PFC model; "prePF" is the prefrontal cortex model before adjustment through subtraction of "Slice" and "true PF" is the real value for the surface are of the PFC. No adjustments to volume were necessary.

Table 4: Measurement results.

Measurement	*Pan troglodytes* (n=8)	*Homo sapiens* (n=3)**	**Percent Difference**	***p*-Value** (Kruskal-Wallis)
PFC Surface Area (cm^2)	132.35 (± 19.60)	441.20 (± 46.84)	70.00	
Cerebrum Surface Area (cm^2)	567.93 (± 70.74)	1906.20 (± 175.00)	76.08	
PFC Volume (cm^3)	53.08 (± 9.94)	137.60 (± 20.63)	61.43	
Cerebrum Volume (cm^3)	262.93 (± 35.22)	1099.35 (± 101.27)	70.20	
(PFC SA : Cerebral SA) x 100	23.37 (± 2.49)	23.14 (± 1.99)	0.98	0.732
(PFC Vol : Cerebral Vol) x 100	20.20 (± 2.66)	12.50 (± 0.73)	61.41	0.017*
PFC SA : PFC Vol	2.52 (± 0.26)	3.21 (± 0.29)	21.38	0.017*
Cerebral SA : Cerebral Vol	2.18 (± 0.26)	1.73 (± 0.10)	25.63	0.053
Relative*** PFC SA : Vol	3.07 (± 0.12)	4.07 (± 0.08)	24.66	0.017*
Relative*** Cerebrum SA : Vol	3.72 (± 0.19)	4.23 (± 0.19)	12.00	0.017*

*Significance $p \leq 0.05$

% Difference = (Chimpanzee-Human)/Human)*100

**Human data is composite from (Tramo 1995, 1998; McBride 1999).

***Relative values = $(SA)^{1/2} : (Vol)^{1/3}$

CHAPTER 5: Discussion

5.1 Introduction

The results of this study indicate that proportionate size of the prefrontal cortex is virtually identical in humans and chimps. The measurements indicate that that PFC accounts for 23% of the total surface area of the cerebral cortex. However, in spite of the similarities, there are gross anatomical differences between the chimpanzee and human prefrontal cortex beyond absolute size. The lower surface area to volume ratio in PFC of the chimpanzee indicates less "foldedness" in this region when compared to humans. Less folding, and correspondingly less white matter in the chimpanzee, could account for the observed difference in cognitive complexity between chimpanzees and humans. The exact relation of foldedness of the PFC to cognitive potential still remains unclear. Thus, it would be unwise to use foldedness as the only evaluative criterion which is why the present study has computed other measures to define a soft tissue, especially neural tissue, in terms of processing ability.

5.2 Theoretical Considerations: Significance of Surface Area to Volume Ratios

The surface area to volume ratio is classically considered in cell theory but also has important implications in engineering. As a shape grows, whether biological or otherwise, the surface area and the volume do not increase in a linear direction. Generally the volume of an object will increase at a much faster pace than the surface area will. This principal sets a natural limit to the size certain shape can become and

still exist. This becomes important in biology with cells as they continue to become larger; they membranes will have trouble structurally containing the increase in internal volume. Processes such as nutrient and waste exchange also reach a natural ceiling as surface area of a cell or tissue will create a bottleneck where only a certain amount of a given substance will be able to cross the surface, through active or passive transport, to deeper tissue per unit of area.

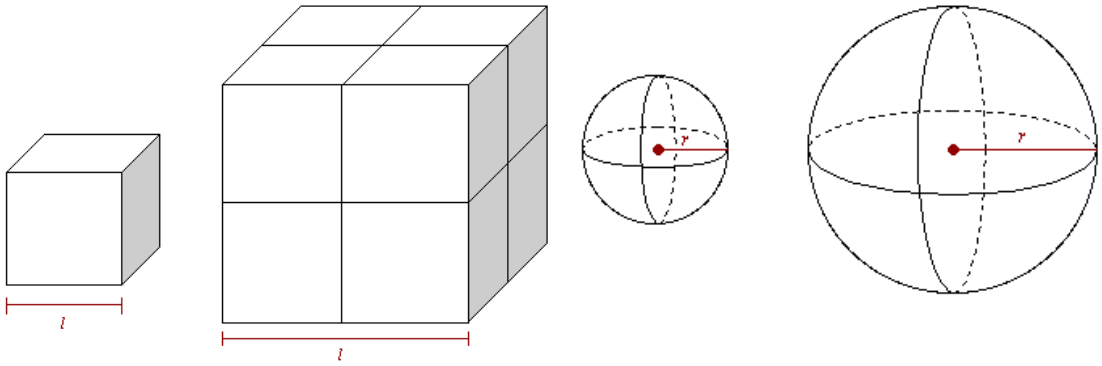

Figure 8: Examples of test shapes.

Using a sphere and a cube as example shapes, we can see how surface area and volume are related to each other as these shapes grow. The formulas for the surface area and volume of a cube are $6l^2$ and l^3 respectively. The formulas for the surface area and volume of a sphere are $4\pi r^2$ and $4\pi r^3/3$ respectively. As demonstrated in Table 5, as the size of the shape increases, the surface area to volume ratio decreases. The surface area to volume ratio can be used as a measure of how convoluted the surface of a shape is. A sphere is a shape maximized to have the least surface area per unit of volume thus is has a lover surface area to volume ratio than a cube does.

In this study we measured the surface area to volume ratio in the prefrontal cortex of chimpanzee (2.52) and human (3.21) brains to be significantly different ($p = 0.017$) from one another. We also measured the surface area to volume ratio of the whole cerebrum of chimpanzee (2.18) and humans (1.73) and found them to be different but not significantly ($p = 0.053$). From these measurements we can see that while the whole cerebrum in the chimpanzee is not significantly different in its convolutions, or foldedness, the PFC is significantly different between the species.

Table 5: Test data on a cube and a sphere of increasing size.

Shape (l or r)	**SA**	**Vol**	**SA:Vol**	**$SA^{1/2}$**	**$Vol^{1/3}$**	**$SA^{1/2}$:$Vol^{1/3}$**
cube 2	24.0	8.0	3.0	4.8990	2.0	2.4495
cube 4	96.0	64.0	1.5	9.7980	4.0	2.4495
cube 6	216.0	216.0	1.0	14.697	6.0	2.4495
cube 8	384.0	512.0	0.75	19.596	8.0	2.4495
sphere 2	50.264	33.509	1.50	7.0897	3.2240	2.1991
sphere 4	201.06	268.08	0.75	14.179	6.4480	2.1991
sphere 6	452.38	904.75	0.50	21.269	9.6719	2.1991
sphere 8	804.22	2144.6	0.375	28.359	12.895	2.1991

It is worthy to note that going from a chimpanzee to a human brain, the surface area: volume ratio of the entire cerebrum gets smaller, which is expected as a brain gets larger. However, the exact opposite is true for the PFC. In this case, the surface area: volume ratio in the PFC gets *larger* as we go from chimpanzee to human. This paradoxical relationship can be accounted for on the basis of cortical surface folding. This is evidence that the PFC in human brains is more folded than scaling would predict

when compared to another great ape. This gross anatomical difference matches the increased functional ability in this region as demonstrated by abnormally complex behavior show by humans.

To correct for unit disagreement and to find a relation between shapes as they increase in size, the square root of the surface area and the cube root of the volume must first be found before the ratio is calculated. This relatedness constant (Vogel 1988) allows evaluation of how similar a shape is without confounding issues of size. Table 5 demonstrates that any cube with a side l will have a relatedness constant of 2.4495 or $[(6l^2)^{1/2}/(l^3)^{1/3}] = 2.4495$. For a sphere with radius r the constant is 2.1991 or $[(4\pi r^2)^{1/2}/(4\pi r^3/3)^{1/3}] = 2.1991$.

These formulas work for simple geometric shapes but the relatedness constant also translates well to more complex biological shapes including the interspecies differences in cortical folding. In this study we found that the calculated relatedness constants for the prefrontal cortex in chimpanzee and human brains, values of 3.07 and 4.07 respectively, were significantly different from one another ($p = 0.017$). It was also found that the relatedness constants for the whole cerebrum in chimpanzee and human, 3.72 and 4.23 respectively, were also significantly different from each other ($p = 0.017$). These relatedness constants are a mathematical way to evaluate shape of an object without size being a factor. The difference in relatedness constants in the PFC and whole cerebrum between chimpanzee and human brains demonstrates that these structures are in fact different shapes and not just scaled versions of one another. Simply stated, the human cerebral cortex and PFC are more heavily convoluted than

found in chimpanzees; the degree of convolution across species accounts for the differences in shape measured as the relatedness constant.

5.3 Implications of Research

The findings of my thesis do not necessarily confirm or negate the previous research on the prefrontal cortex in human and nonhuman primates. The disagreement over the relative size of the prefrontal cortex in chimpanzees and how it compares to the human brain may benefited by the larger sample size in my study. The lack of cytoarchitectural data corresponding to surface landmarks led to my use of methodological boundaries as employed by previous researchers (Semendeferi et al., 2001, 2002, Schoenemann et al., 2005). This fact alone may be the source of the conflicting findings but keep in mind that a very careful test-retest reliability analysis found that the experimental error with such operational boundaries in low and within 0.45-2.65%. However, because the reliability error in estimating the entire cortex was also determined to be lower (i.e., 0.49-0.54%) it must be concluded that clear anatomical boundaries (present in measuring the entire cortex and in some question in measuring the PFC) is an important source of experimental error. Future studies employing measurements of the PFC in which the actual boundaries are defined cytoarchitecturally will be required to resolve the final issue of functional boundaries of PFC in chimpanzees and other nonhuman primates.

Cortical surface area alone does not appear to be an important experimental variable in evaluating evolutionary changes in brain function. Indeed, in spite of major behavioral and cognitive differences between man and chimpanzee, the relative size of

the area responsible for complex cognitive and behavioral tasks (the prefrontal cortex) in the two species is identical. Future studies will need to concentrate on other structural differences to account for intraspecific variation. This study has shown that subtle changes in cortical folding patterns, measured as surface area: volume ratios could account for the noted cognitive changes across species. Obviously a more detailed study using clearly defined cytoarchitectural boundaries between the prefrontal and the rest of the frontal cortex will give a better representation of the region that sulcal morphology alone cannot. Beyond evaluation of the adult structure in humans and non human primates, an investigation into the developmental processes that drive the brain to increase its size or foldedness is warranted. By determining which factors affect both the size and shape of adult neural tissues, the factors that selection acted upon during human neural evolution can be better understood. An understanding of these differences and developmental processes will tell us more about the structural basis for known functional differences, and help future research form testable hypotheses about the evolutionary mechanisms responsible for human brain evolution.

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