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Strategies for Explaining Species Difference in Human/Ape Comparative Neuroanatomy

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by

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ABSTRACT OF THE THESIS

Strategies for Explaining Species Difference in Human/Ape Comparative Neuroanatomy

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There is a great deal of interest in understanding cognitive and behavioral differences between humans and other primates. One way to do this is to investigate the evolution of the neurological substrates underlying these cognitive and behavioral differences. Once these species differences have been identified they must be interpreted, and different explanatory strategies have been proposed for this purpose, though not strictly in the context of human/ape comparisons. This paper therefore reviews findings from comparative neuroanatomical studies of humans and apes from the last twenty-five years at both the macro- and micro structural levels, along with three strategies for explaining species difference. These strategies are mechanical,

developmental, and adaptational explanations. Finally, what these categories mean for, how they apply to, and how they intersect in human/ape comparative neuroanatomical work is discussed in the context of the reviewed findings.

Introduction

Understanding the histories and origins of the similarities and differences in the morphological and behavioral features of humans and other primates requires an evolutionary perspective and spans many fields and bodies of literature. Naturally, there is a great deal of interest in understanding cognitive and behavioral differences, as well as the neurological substrates underlying these differences, between humans and other primate species. The focus of this paper will therefore be on the neurological aspects of primate evolution and the strategies that can be used to explain neurological differences observed between species.

Towards that end, this paper will begin with an account of some of the approaches for data collection employed in comparative neuroanatomical studies. This discussion will center on histologically- and neuroimaging-based methods as these are the noninvasive methods available, and frequently employed, in comparative analyses of human and non-human primate brains. In addition to this, this paper will review some of the major findings of comparative neuroanatomical studies from the last twenty-five years with a particular focus on those findings related to the neural substrates of cognition. Additionally, the findings reviewed here will focus primarily on human-ape comparisons. However, some comparisons with other primate species, especially macaques, will also be discussed since they are often included in studies which compare humans and apes.

As with any science, interpretation of data plays a key role in comparative neuroanatomy. In this particular case, the data to be interpreted is related to differences in neural characteristics between humans and other primate species. Various strategies for explaining species difference have been proposed at different times (Amundson, 1994; Gould & Lewontin, 1979; Maynard Smith et al., 1985) and these strategies have been pulled together into three broad categories;

mechanical, developmental, and adaptational explanations (Striedter, 2005). Mechanical explanations understand species-difference in terms of the constraining effects of certain mechanical considerations (Gould & Lewontin, 1979; Striedter, 2005). Developmental explanations appeal to the constraining effect certain rules of neural development may have on the evolution of the primate brain (Amundson, 1994; Gould & Lewontin, 1979; Maynard Smith et al., 1985; Striedter, 2005). Finally, adaptational explanations account for species-difference as the result of selection for a particular behavior which results in the emergence of a related neural characteristic (Amundson, 1994; Gould & Lewontin, 1979; Striedter, 2005). This final strategy has been quite frequently employed in the past, particularly as regards brain regions related to language processing (Falk, 1980; Hewes et al., 1973; Parker & R., 1979). That is, the evolution of these regions in humans has been explained as a result of selection for behaviors related to language production and processing. However, purely adaptational explanations have been criticized for their reliance on plausibility rather than evidence, and their failure to consider or account for other factors (i.e. mechanical or developmental constraints) in the evolution of particular neural characteristic (Gould & Lewontin, 1979). This paper will explore these strategies in the context of the neuroanatomical findings in humans and apes from the last twenty-five years in order to see what these categories mean for, how they apply to, and how they intersect in human/ape comparative neuroanatomical work.

Approaches for Collecting Data

Before beginning any discussion of explanatory strategies, it is first necessary to review different approaches for data collection in comparative neuroanatomical studies. It is not sufficient to study only the relationship of total brain to body size (Semendeferi, Barger, &

Schenker, 2010). Indeed, the specific neural circuits and brain areas of closely species must also be studied (Semendeferi et al., 2010). The methods available for such comparative studies fall primarily into two categories. These are methods which can be employed at the macrostructural level, and methods which can be employed at the microstructural level. Macrostructural approaches to studying the brain rely on imaging technologies and can be further divided into two categories, structural and functional neuroimaging. Structural imaging, as the name suggests, facilitates the analysis of structures of the brain identifiable at a gross anatomical level. Functional imaging also deals with brain regions identifiable at a gross anatomical level, however it is used to analyze the function of a particular region. While both methods will be discussed in more detail later on, this paper will focus on findings obtained using structural imaging techniques.

Microstructural approaches to studying the brain rely on different staining techniques. Different techniques allow for the visualization of different aspects of brain microstructure. This paper will review studies which employ Nissl and Gallyas, immunohistochemical, myelin, and Golgi stains. These stains are used to visualize cell bodies, specific subpopulations of cells, myelinated fibers, and dendritic arbors respectively. As was the case with macrostructural approaches above, each of these methods will be discussed in more detail later on.

Neuroanatomical Findings in Human/Ape Studies

Before beginning this section, it should be noted that more detailed information (regions of interest, number and age of subjects, and methods) about the studies discussed here can be found in the accompanying table.

Macrostructural Approaches

As previously stated, macrostructural approaches to studying the brain can be divided into structural and functional imaging techniques. Structural neuroimaging techniques include structural magnetic resonance imaging (MRI) and diffusion tensor imaging (DTI). MRI measures the amount of water present in different tissue and allows for better visualization of soft tissue. DTI measures the diffusion of water molecules along axons and can be used to visualize white matter tracts. Functional neuroimaging techniques include functional MRI (fMRI) and positron emission tomography (PET). Functional MRI measures blood flow and oxygen use during the performance of a task in order to see what regions are active. Similarly, PET measures metabolic activity, physiology, and blood flow using an exogenous tracer. Although both fMRI and PET have been employed in comparative studies with primates, more comparative work has been conducted using structural imaging techniques and this paper will focus on findings obtained using these methods. It should also be noted that while neuroimaging is very useful in comparative neuroanatomical studies it is not without its limitations. These techniques cannot be used to identify or investigate cortical areas as defined by Brodmann and others. Instead, these techniques must be used to investigate regions of the brain identifiable based on gross anatomical landmarks.

Macrostructural Literature

The following section reviews human/ape neuroanatomical findings obtained through the use of structural imaging techniques and, for the sake of clarity, this literature has been divided according to functional systems. That is, brain regions involved in executive functioning, speech and language, learning and memory, and socioemotional processing. Additionally, there is a fifth

section which deals with findings than cannot be easily placed into any one of these discrete categories.

Executive Functioning

Brain regions involved in executive functions have been frequent targets of study for comparative neuroanatomical studies (Aldridge, 2011; Donahue, Glasser, Preuss, Rilling, & Van Essen, 2018; Hopkins & Avants, 2013; Hopkins, Li, Crow, & Roberts, 2017; Sakai et al., 2013; Sakai et al., 2011; Schenker, Desgouttes, & Semendeferi, 2005; Semendeferi & Damasio, 2000). At the macrostructural level these are primarily focused on grey and white matter volumes, cortical thickness, and gyrification of the frontal lobe.

MRI

Semendeferi and Damasio (2000) used *in vivo* MRI to investigate the overall brain size in hominoid species, as well as the relative size of large sectors of the brain. These sectors included frontal, temporal, parieto-occipital, and insular regions of the cerebrum as well as the cerebellum. Results of this study indicated that the frontal lobe in humans is not larger than expected in an ape of human brain size. However, the frontal lobe of the gibbon is small in comparison to the great apes. This result is significant since unique human cognitive abilities had previously be attributed to a differentially enlarged frontal lobe (Semendeferi & Damasio, 2000). A similar study therefore investigated the relative volumes of subsectors of the frontal lobe to test the idea that neural reorganization took place. Frontal lobe white matter was parcellated into gyral (immediately beneath the cortex) and core (everything else) white matter and the relationship between cortex and gyral white matter was analyzed in the dorsal, mesial, and

orbital sectors of the frontal lobe. Results of this study also demonstrated homogeneity between humans and apes and almost all regions examined were as large as expected. However, in humans gyral white matter volume is larger than expected for an ape of human brain size and the two *Pan* species have a larger ratio of gyral white matter to cortex compared with *Gorilla* and *Pongo* in the dorsal sector of the frontal lobe. Additionally, the orbital sector in the frontal lobe of orangutans was smaller than in the other species, and the dorsal sector of the frontal lobe in chimpanzees is larger than in bonobos (Schenker et al., 2005). Moreover, Aldridge (2011) conducted whole brain analyses on humans, chimpanzees, bonobos, gorillas, orangutans, and gibbons using 29 anatomical landmarks to determine whether a specific suit of features distinguishes the morphology of the human brain from other apes. The results showed patterns of morphology, in other words spatial relationships between the 29 landmarks used in this analysis, that were consistently different between humans and all ape species, as well as patterns that differed among ape species. The pattern consistent between all apes and humans indicated, among other things, a change in relationships between cortical and subcortical frontal structures (Aldridge, 2011).

Within the frontal lobe, the prefrontal cortex is frequently studied in comparative contexts due to its important role in executive functions. However, it is difficult to study the prefrontal cortex at a macrostructural level because its borders can only be estimated based on gross morphological landmarks. Donahue et al. (2018) present two parcellation-based delineations of the prefrontal cortex and demonstrate that previously used delineations underestimate the extent of the prefrontal cortex, especially in humans. They found that the proportion of grey matter occupied by the prefrontal cortex in humans is 1.2-fold greater than in chimpanzees and 1.9-fold greater than in macaques. This disparity is even more prominent in

prefrontal white matter. The proportion of white matter underlying the prefrontal cortex is 1.7-fold greater in humans than chimpanzees and 2.4-fold greater in humans than macaques (Donahue et al., 2018). Additionally, differences in the development of prefrontal white matter have been investigated in humans and chimpanzees (Sakai et al., 2011). In this case longitudinal MRI data was collected from 3 chimpanzees at regularly scheduled intervals between the ages of 6 months and 6 years and compared to previously collected data from humans between the ages of 1 month and 10.5 years. Since prefrontal regions cannot be accurately identified on MR images the coronal slice anterior to the corpus callosum was used to consistently divide prefrontal from non-prefrontal regions. It was observed that prefrontal white matter volume in chimpanzees, like humans, has not reached adult values during prepuberty. However, the rate of prefrontal white matter volume increase during infancy is slower in chimpanzees than in humans (Sakai et al., 2011).

Along similar lines, longitudinal MRI data was collected from 3 chimpanzees from the ages of 6 months to six years and compared to cross sectional MRI data collected from 28 humans between the ages of 1 month to 10.5 years. This data was used to calculate total cerebral volume as well as grey and white matter volumes during development in humans and chimpanzees. This study revealed similarly protracted cerebral development during prepuberty in chimpanzees. However, in humans there is a rapid increase in cerebral volume driven by a dramatic increase in white matter volume that is not observed in chimpanzees (Sakai et al., 2013). Across the entire cortex measurements of cortical thickness, white matter volumes, and gyrification have been compared in humans and chimpanzees. Results indicated that humans generally display greater gyrification and thinner cortex than chimpanzees. This was particularly evident in the frontal lobe. Additionally, frontal lobe white matter volumes were also higher in

humans. This was particularly evident in prefrontal sectors of the frontal lobe, though it should be noted that the prefrontal cortex itself cannot be reliably identified at the macrostructural level (Hopkins et al., 2017). Along similar lines, Hopkins and Avants (2013) compared MRI data from chimpanzees to previously obtained human data to investigate the relationship between cortical thickness, volume, and surface area. Cortical thickness was calculated for several areas identifiable across species, along with surface area, grey matter volume, and white matter volume for each hemisphere. They found that regional variation in cortical thickness is significant in chimpanzees. Primary motor and sensory areas have lower values compared to association cortex. Additionally, cortical thickness was found to be negatively correlated with white matter volume (Hopkins & Avants, 2013).

Overall, these studies indicate a certain degree of reorganization in the regions involved in executive functioning in humans. These differences seem particularly evident in human prefrontal regions. However, given the level of detail available with imaging technologies, prefrontal borders can only be estimated.

Speech and Language

Another set of brain regions of frequent interest in comparative studies are those related to speech and language in humans and their homologues in nonhuman primates (Aldridge, 2011; Ardesch et al., 2019; Hopkins & Avants, 2013; Hopkins, Lyn, & Cantalupo, 2009; Rilling et al., 2007; Rilling & Seligman, 2002; Semendeferi & Damasio, 2000). These include areas of the frontal and temporal lobes containing Broca's and Wernicke's areas (and their homologues) along with the connections between these regions.

MRI

The study conducted by Semendeferi and Damasio (2000) mentioned above indicates that the human temporal lobe might be larger than expected for an ape of human brain size However, the sample size was small, and these results did not reach statistical significance (Semendeferi & Damasio, 2000). However, the whole brain analysis of humans and apes discussed previously also indicated an expansion of the temporal lobe in humans (Aldridge, 2011). Additionally, a study conducted by Rilling and Seligman (2002) which measured temporal lobe, superior temporal gyri, and temporal lobe white matter volume in 44 anthropoid primate species determined that the volume of the human temporal lobe is larger than expected. Moreover, they found that human temporal lobe white matter volume is larger than predicted for brain size and predicted for temporal lobe volume (Rilling & Seligman, 2002).

Hopkins, Lyn, and Cantalupo (2009) also investigated the homologues of Broca's and Wernicke's areas in chimpanzees and bonobos through volumetric estimates of the inferior frontal gyrus and planum temporale respectively. Their results show that there are no significant differences between species in the inferior frontal gyrus and planum temporale (Hopkins et al., 2009). However, some of the regions investigated by Hopkins and Avants (2013) in chimpanzees included regions homologous to those involved in speech and language in humans (see table). For each of these regions cortical thickness was calculated, along with surface area, grey matter volume, and white matter volume for each hemisphere. They found regional variation in cortical thickness is significant in chimpanzees. Primary motor and sensory areas have lower values compared to association cortex. Additionally, cortical thickness was found to be negatively correlated with white matter volume (Hopkins & Avants, 2013).

DTI

In addition to social learning, mirror self-recognition may be related to communication abilities and the development of language. The study conducted by Hecht et al. (2017) which determined that successful self-recognition is associated with rightward asymmetry in the white matter of SLF II and III, as well as the grey matter termination of SLF III, and that chimpanzees with more human-like SLF connectivity exhibited more human-like behaviors is also relevant for a discussion of regions associated with speech and language. Another white matter tract involved in language processing is the arcuate fasciculus; the white matter tract connecting Broca's and Wernicke's areas. An investigation of the arcuate fasciculus in humans, chimpanzees, and macaques revealed a prominent temporal lobe projection in humans which was not present in either of the other two species studied (Rilling et al., 2007)

Finally, a general analysis of white matter connectivity in humans and chimpanzees reveals particular links between multimodal areas of the temporal, lateral parietal, and inferior frontal cortices, including tracts which are important in language processing. Furthermore, network analysis demonstrates that these connections are responsible for particularly high contributions to global network integration in the human brain (Ardesch et al., 2019).

Learning and Memory

Brain regions involved in learning and memory have also been frequently studied from a comparative perspective (Hecht, Gutman, Bradley, Preuss, & Stout, 2015; Hecht et al., 2013; Hecht et al., 2017; Hopkins et al., 2009; Pope, Taglialatela, Skiba, & Hopkins, 2018). At the macrostructural level these include the hippocampus, regions of the striatum, and connections between frontal, parietal, and temporal regions.

MRI

A study conducted by Hopkins, Lyn, and Cantalupo (2009) investigated the neural substrates underlying behavioral and cognitive differences in chimpanzees and bonobos through volumetric estimates of several regions (see table), including the hippocampus and striatum, in these species. The results indicate that the chimpanzee hippocampus and putamen are borderline significantly larger than in bonobos. Whereas there are greater leftward asymmetries in the bonobo striatum (Hopkins et al., 2009).

DTI

Social learning techniques, linked to the mirror system, also differ between primate species. Humans and chimpanzees will copy the processes employed to achieve a particular task, while macaques will only copy the product. Both *in vivo* and postmortem DTI scans of humans, chimpanzees, and macaques have been used to investigate the relationship between mirror system connectivity and social learning techniques employed by these species. Manually traced ROIs were used to seed tractography to ensure that all streamlines started in grey matter, and results indicate most mirror system circuitry in chimpanzees (and macaques) consists of frontal-temporal connections. In humans there is more substantial temporal-parietal and frontal-parietal connections. In both humans and chimpanzees mirror system circuitry includes connections with the inferior temporal cortex, and in humans alone it includes connections with the superior parietal cortex (Hecht et al., 2013).

The superior longitudinal fasciculus (SLF), which connects frontal and parietal regions and may be related to neural circuits involved in social learning, has been investigated using DTI scans of humans and chimpanzees. SLF I, the most superior branch of the SLF, shows similar

patterns of connectivity in humans and chimpanzees and is volumetrically larger in chimpanzees than in humans. SLF II, the middle branch, shows greater connectivity with the dorsolateral prefrontal cortex in humans and greater connectivity with the inferior frontal gyrus in chimpanzees. SLF III, the inferior-most branch, is right lateralized and volumetrically larger in humans. Additionally, SLF III in humans shows reduced connectivity with the dorsal premotor cortex and increased projection into the anterior inferior frontal gyrus (Hecht et al., 2015). Finally, mirror self-recognition is a cognitive skill demonstrated by humans and shared with only a few other species, including chimpanzees. Mirror self-recognition involves cortical areas in the frontal and parietal regions. Moreover, mirror self-recognition is highly variable in chimpanzees. Hecht et al. therefore investigated the relationship between mirror self-recognition and the anatomy of the SLF in chimpanzees using DTI. A virtual dissection of the SLF was carried out and results indicate that successful self-recognition is associated with rightward asymmetry in the white matter of SLF II and III, as well as the grey matter termination of SLF III. However, the asymmetries are not seen at the population level in chimpanzees as they are in humans. Moreover, chimpanzees with more human-like SLF connectivity exhibited more human-like behaviors (Hecht et al., 2017).

Taken together these finding indicate changes in the connectivity between frontal, parietal, and temporal regions in humans compared to other apes. These changes may be related to learning abilities in humans but, given the diverse functions of the regions mentioned here, this cannot be definitely asserted.

Socioemotional Processing

Regions involved in socioemotional processing are also of interest from a comparative neuroanatomical perspective (Aldridge, 2011; Rilling et al., 2012). In particular regions of the insular and cingulate cortices, the amygdala, and connections between these regions.

The study conducted by Aldridge mentioned above which analyzed whole brain morphological differences between humans and apes also reveals a chance in the location of amygdala in the uniquely human pattern of morphology (Aldridge, 2011). Comparative analyses of regions involved in socioemotional processing are particularly interesting in chimpanzees and bonobos given the behavioral differences which can be observed between these species. Rilling et al. (2012) investigated possible neurological correlates of these differences using both *in vivo* and postmortem DTI and MRI scans. Manually traced ROIs were used to seed tractography in the DTI scans and MRIs were used to estimate grey matter volume in specific brain areas Results show that bonobos have more grey matter in brain areas important in perceiving distress, as well as a larger path linking the amygdala and ventral anterior cingulate cortex. This pathway is implicated in top-down control of aggressive impulses, as well as bottom-up biases against harming others (Rilling et al., 2012).

Whole Brain Analyses

As can be seen in some of the studies discussed above, it is possible to conduct whole brain analyses at the macrostructural level. In the previously mentioned studies, findings were discussed in the context of specific functional systems. However, this need not always be the case as will be seen with the studies discussed in this section (Chen et al., 2013; Hopkins, Li, & Roberts, 2019; Li et al., 2017).

An investigation which focused specifically on cortical folding patterns in humans and other primate species used *in vivo* MRIs of humans, chimpanzees, and macaques. Cortical folding patterns of each species were described using hinge numbers. Comparisons of folding patterns identified 6 common three-hinge gyral folds across species, 6 that were unique to chimpanzees and 14 unique to humans (Li et al., 2017). In another investigation of cortical folding patterns, using both MRI and DTI, Chen et al. (2013) determined that structural fiber connection patterns closely follow gyral folding pattern in the direction tangent to the cortical sphere in all species studied, despite increases in complexity and variability of folding and fiber patterns.

Finally, a study by Hopkins, Li, and Roberts (2019) investigated the relationship between general intelligence and aspects of cortical organization, including total brain volume, total grey matter volume, mean cortical thickness, and regional variation in cortical thickness and grey matter volume. Their results show that increased grey matter volume and cortical thickness may be computationally more effective in basic cognitive processes (Hopkins et al., 2019).

Microstructural Approaches

As previously stated, microstructural approaches to studying the brain involve the use of different staining techniques and the literature discussed here employs four different techniques. These are Nissl and Gallyas stains, various immunohistochemical stains, myelin stains, and Golgi stains. Nissl and Gallyas stains allow for the visualization of all cell bodies (neurons, glia, and endothelial cells). This kind of stain can be used to investigate total neuron numbers, neuronal densities, neuropil space, and grey-level indices (GLI). Total neuron counts, as the name suggests, are estimations of the total number of neurons in a given area obtained using

certain stereological sampling techniques (Semendeferi, Armstrong, Schleicher, Zilles, & Van Hoesen, 2001). Neuronal densities are obtained similarly, the difference is that neuronal densities express the ratio of total neuron number to total volume of a given area (Semendeferi, Damasio, Frank, & Van Hoesen, 1997). Neuropil is the space between cell bodies occupied by axons, dendrites, synapses, glial cell processes, and microvasculature (Spocter et al., 2012). It can therefore be used as a proxy for the connectivity in a given area (Spocter et al., 2012). The GLI is similar to the neuropil fraction and GLI values obtained by summing all of the cell bodies and dividing by the total space (Semendeferi et al., 2001; Spocter et al., 2012; Zilles, Schleicher, & Kretschmann, 1978). Therefore a lower GLI value represents more space for connections (Semendeferi et al., 2001). Immunohistochemical methods are used to target specific populations of cells and axonal fibers so that the presence, absence, or and amount of these subpopulations can be compared between both different areas and different species. Myelin stains target white matter and allow for the investigation of aspects of microstructure related to myelinated axons. Lastly, Golgi stains selectively stain entire neurons and allow for the analysis of dendritic branching. The above methods are useful for investigating reorganization of specific functional areas in the brain, however issues due to tissue fixation and shrinkage can arise with these methods.

Microstructural Literature

The following section reviews human/ape neuroanatomical findings obtained using the staining techniques discussed above and, as was the case with the macrostructural literature, this literature has been divided according to functional systems. That is, brain regions involved in future planning, speech and language, learning and memory, and socioemotional processing.

Future Planning

Regions involved in future planning and the undertaking of initiatives have frequently been the object of comparative neuroanatomical studies. In particular, area 10 in humans and other primates has been extensively studied for its role in these functions (Bianchi, Stimpson, Bauernfeind, et al., 2013; Bianchi, Stimpson, Duka, et al., 2013; Miller et al., 2012; Semendeferi et al., 2001; Semendeferi et al., 2010; Smaers, Schleicher, Zilles, & Vinicius, 2010; Smaers et al., 2011; Spocter et al., 2012; Teffer et al., 2013).

Nissl and Gallyas staining

Several cytoarchitectonic features of area 10 have been investigated using Nissl-stained sections from humans, other apes, and macaques. In each species the volume, GLI, relative size of cortical layers, and cortical counts were obtained. Results indicate that area 10 in humans is larger relative to the rest of the brain relative to other apes. Additionally, there is more space available for connections in area 10, specifically in the supragranular layers (Semendeferi et al., 2001).

Analysis of spatial organization of neurons in area 10 in humans and other apes indicate that the horizontal spacing distance (HSD), which is the average spacing between neurons for the area, of neurons in area 10 is greater in humans than other apes. Grey-level ratio (GLR), which represents fraction of space occupied by cell bodies, is correspondingly lower in area 10 in humans compared to other apes (Semendeferi et al., 2011). Additionally, spatial organization of neurons during development has been investigated in various cortical areas (see table) of humans and chimpanzees. For each cortical area analyzed the HSD and GLR of layer III neurons were measured. In both humans and chimpanzees HSD in BA 10 was significantly higher in

postweaning specimens, while no significant age-related differences were found in the other cortical areas (Teffer et al., 2013).

Distribution of neuropil in various cortical areas (see table) in chimpanzees has been investigated by determining the neuropil fraction of Nissl-stained sections from these areas. This data was then compared to data from archival human subjects. Results demonstrate that BA 10 in humans have a significantly higher neuropil fraction than other areas. This was not the case in chimpanzees (Spocter et al., 2012).

An analysis of frontal and non-frontal white and grey matter in 18 anthropoid species reveals that the hyperscalling of the neocortex and frontal lobe to the rest of the brain is largely due to changes in frontal white matter. Moreover, changes in frontal lobe white matter are linked to changes in the rest of the brain and basal ganglia (Smaers et al., 2010). Finally, volumetric estimates of the prefrontal cortex using Nissl-stained sections from humans, other apes, and several monkey species reveal different scaling coefficients in the right versus left prefrontal region. This suggests that left hemispheric prefrontal hyperscaling is a primary factor underlying primate brain evolution with humans at the extreme end of this trend (Smaers et al., 2011).

Myelin and Golgi staining

Myelin stains have been used to investigate the ontogenetic progression of myelination in humans and chimpanzees. Myelinated axon length density was calculated throughout development in various cortical areas of humans and chimpanzees. Subjects ranged in age from birth to adulthood. Results indicate that density of myelinated axons in chimpanzees increased steadily throughout development with adult-like levels being reached around the time of sexual

maturity. However, humans display a slower development through childhood with a delayed period of maturation that extends beyond late adolescence (Miller et al., 2012).

Additionally, in humans and chimpanzees the rapid Golgi method was used to quantify layer III pyramidal neurons in several cortical areas. Ten layer III, pyramidal neurons were isolated in each area for each subject. Results indicate greater dendritic complexity in area 10 of both humans and chimpanzees that was not present in other cortical areas. However, in humans pyramidal neurons display longer, more complex branching in all cortical areas examined (Bianchi, Stimpson, Bauernfeind, et al., 2013). Another study used Golgi staining to investigate the development of dendritic morphology in chimpanzees and compared these data to similar findings in humans. Results show that pyramidal neurons in the prefrontal cortex develop later than those in other cortical areas. This is consistent with similar data collected in humans (Bianchi, Stimpson, Duka, et al., 2013).

Taken together these studies indicate an expansion of area 10 in humans between humans and other primates, as well as some differences between nonhuman primate species. This increase seems to be driven by increased connectivity of area 10.

Speech and Language

A number of studies investigating brain regions related to speech and language have also been conducted at the microstructural level (Buxhoeveden, Lefkowitz, Loats, & Armstrong, 1996; Buxhoeveden, Switala, Roy, Litaker, & Casanova, 2001; Palomero-Gallagher & Zilles, 2019; Raghanti et al., 2016; Schenker et al., 2008; Spocter et al., 2010). Cortical areas 44, 45, and 22 in particular have been frequent objects of study for such investigations (Palomero-Gallagher & Zilles, 2019; Schenker et al., 2010; Spocter et al., 2010). Areas 44 and 45 are also

known as Broca's area and have been implicated in language production in humans (Schenker et al., 2010). Area 22 is also known as Wernicke's area and has been implicated in language comprehension (Spocter et al., 2010). Certain subcortical structures, namely the basal ganglia, have also been investigated in relation to the neurological substrates underlying speech and language (Raghanti et al., 2016). The basal ganglia has been implicated in speech production, sentence comprehension, and the processing of grammar and syntax (Raghanti et al., 2016).

Nissl and Gallyas staining

Minicolumnar organization in Broca's area (BA 44 and 45) has been investigated in humans and great apes. Nissl-stained sections from humans and other apes were used to estimate HSD and grey-level index GLI in layer III of Broca's area. Results indicate that there were no population-level asymmetries in HSD or GLI. However, GLI is higher in humans than in the great apes. HSD in humans is also greater in terms of absolute size, but smaller than the great apes relative to brain size (Schenker et al., 2008). Palomero-Gallagher and Zilles (2019) also investigated the neuronal organization of Broca's area in humans, other ape species, and macaques. They used Nissl-stained sections from humans, other apes, and monkeys to calculate layer-specific GLIs in BA 44 and 45. Their results indicate that humans had the largest neuropil volume, the great apes have lower neuropil volume, and macaques have the lowest neuropil volume. This suggests more space for connections in human BA 44 and 45 than in the other primate species (Palomero-Gallagher & Zilles, 2019).

In Wernicke's area, linear organization of area Tpt has been studied in adult humans, chimpanzees, and macaques, and compared to the prelaminated fetal cortical plate. Results show that the arrangement of cells in layers III and, to a lesser extent, V closely resemble the fetal

template in all species, while arrangement of cells in layers II and IV diverge from this template. Cell density is less in the species with larger brains and this difference is largely due to an increase in distance between cell columns. Additionally, horizontal distance is widest in humans and this distance in most pronounced in layer II and least pronounced in layer III (Buxhoeveden et al., 1996). Additionally, minicolumnar organization of the planum temporale, the heart of Wernicke's area, has been investigated in humans, chimpanzees, and macaques. Results of this analysis reveal wider minicolumns and more neuropil space in the left hemisphere in humans (Buxhoeveden et al., 2001). Another study used Nissl-stained sections of chimpanzees to estimate regional volumes, total neuron numbers, and neuron density of area Tpt. They found a population-level leftward asymmetry in total neuron number, as well as a volumetric asymmetry approaching significance. Moreover, asymmetry in neuron numbers in area Tpt was positively correlated with an asymmetry in neuron numbers in BA 45, a component of Broca's area (Spocter et al., 2010).

Immunohistochemical staining

The basal ganglia have also been implicated in speech and language in humans and dopaminergic innervation of the basal ganglia has therefore been investigated in humans, other apes and monkey. The densities of tyrosine hydroxylase immunoreactive (TH-ir) axons in five regions of the basal ganglia were calculated as a measure of dopaminergic innervation in these species. Results indicate that there is an increase of dopaminergic innervation in the medial caudate nucleus in humans compared to the other species studied. Moreover, there was no change in dopaminergic innervation in chimpanzees that used socially learned attention-getting sounds compared to those that did not (Raghanti et al., 2016).

Overall these results showed an increase in neuropil space in cortical regions associated with speech and language in humans compared to apes. Asymmetries in neuron number and density were observed in both humans and apes. Additionally, there is an increase in dopaminergic innervation in the human basal ganglia.

Learning and Memory

Brain regions involved in learning and memory have also been studied in a comparative context (Raghanti et al., 2011; Raghanti et al., 2009; Raghanti et al., 2008a, 2008c, 2008d; Stephenson et al., 2017). In the frontal cortex area 9 has been frequently studied due to its role in working memory (Raghanti et al., 2009; Raghanti et al., 2008a, 2008d). Other brain regions implicated in learning and memory which have been studied in humans and nonhuman primates include the basal ganglia and brainstem (Raghanti et al., 2011; Stephenson et al., 2017).

Immunohistochemical staining

Immunohistochemical staining has been used extensively in regions related to learning and memory. Cortical serotonergic innervation was analyzed in humans, chimpanzees, and macaques. SERT-ir axons were quantified in four cortical areas of each of the species studied. Results show that there is no quantitative increase in serotonergic innervation in the human frontal cortex compared to chimpanzees and macaques. However, humans and chimpanzees display greater SERT-ir axon densities relative to neuron densities in layers V/VI in areas 9 and 32. Moreover, axon coils can be observed in humans and chimpanzees, but not in macaques (Raghanti et al., 2008d).

Similarly, dopaminergic innervation of the cortex was compared among humans, chimpanzees, and macaques. TH-ir axon densities were calculated in four cortical areas of each species. Results show that there is no quantitative increase in dopaminergic innervation in humans compared to the other species. However, humans show a sublaminar pattern of innervation in layer I of areas 9 and 32 which is not present in the other species. Both humans and chimpanzees display an increase in dopaminergic innervation in layers III, V/VI in areas 9 and 32 which is not present in macaques. Moreover, axon coils, which may be related to cortical plasticity events, can be observed in humans and chimpanzees, but not in macaques (Raghanti et al., 2008b). A related study measured TH-ir interneurons in areas 9 and 32 in humans, other apes, and several monkey species. In humans, as well as Old World monkeys and the siamang, TH-ir neurons are present in layers V/VI and the white matter below. TH-ir neurons are also observed occasionally in humans, the siamang, and some of the monkey species. TH-ir cells are noticeably absent in the cortex of the great ape species studied. Additionally, humans and the monkey species both show a bilaminar pattern of TH-ir axon distribution in the prefrontal regions. Layers I/II and V/VI in humans and monkeys have the highest TH-ir axon density. In the great apes TH-ir axons were most dense in layer III (Raghanti et al., 2009).

Finally, cholinergic innervation has been studied in the cortex of humans, chimpanzees, and macaques. ChAT-ir axons were quantified in four cortical areas of each of the species studied. Findings reveal no quantitative differences between the cortical areas examined in any species. However, clusters of cholinergic fibers can be observed in humans and chimpanzees but not macaques (Raghanti et al., 2008a).

Subcortical structures and brainstem nuclei related to learning and memory have also been studied using these methods. Cholinergic innervation of the basal ganglia in humans, other apes, and monkeys was investigated by measuring axons and interneurons immunoreactive for choline acetyltransferase (ChAT). Morphology of ChAT immunoreactive (ir) interneurons was also compared across species. Results indicate that humans and great apes have a preponderance if multipolar ChAT-ir interneurons in the caudate nucleus and putamen, while monkeys display a heterogenous mix of multi-, bi-, and unipolar interneurons. Differences in ChAT-ir axon and interneuron densities are observed in the dorsal caudate, putamen, and globus pallidus, but these differences are not associated with the phylogenetic structure of the species studied (Stephenson et al., 2017). Finally, long projection axons from the nucleus basalis provide cholinergic innervation to the neurons of the cerebral cortex. Raghanti et al. therefore investigated total numbers of ChAT-ir magnocellular neurons in nucleus basalis of humans, apes, and monkeys. Results indicated that changes in the cholinergic system among primate species involve axon terminations in the neocortex rather than in subcortical neurons providing innervation (Raghanti et al., 2011).

Brain regions associated with learning and memory also display a number of differences between species. Immunohistochemical staining techniques reveal differences in serotonergic, dopaminergic, and cholinergic innervation of both cortical and subcortical regions associated with learning and memory in humans and other primates. A number of these differences seem to be shared between humans and chimpanzees, but not with macaques.

Socioemotional Processing

Regions involved in socioemotional processing have also been investigated in comparative neuroanatomical contexts (Armstrong, 1980; Armstrong, Clarke, & Hill, 1987; Barger et al., 2012; Barger, Stefanacci, & Semendeferi, 2007; Bauernfeind et al., 2013; Hof, Nimchinsky, Perl, & Erwin, 2001; Issa et al., 2019; Lew et al., 2019; Rogers et al., 2018; Semendeferi, Armstrong, Schleicher, Zilles, & Van Hoesen, 1998; Stimpson et al., 2016). The amygdala is one of the more frequently studied regions when it comes to socioemotional processing due to its critical role in primate emotional and social behavior (Barger et al., 2012; Issa et al., 2019; Lew et al., 2019; Stimpson et al., 2016). However other regions such as the anterior cingulate, insular, and orbitofrontal cortices have also been studied in relation to socioemotional processing (Bauernfeind et al., 2013; Issa et al., 2019; Rogers et al., 2018; Semendeferi et al., 1998). The anterior cingulate cortex has, among other things, been implicated in cognitive functions such as empathy and emotion (Issa et al., 2019). The insular cortex too has been implicated in functions such as empathy and awareness of emotions (Bauernfeind et al., 2013). The orbitofrontal cortex, specifically area 13, is responsible for emotional reactions to social stimuli (Semendeferi et al., 1998).

Nissl and Gallyas staining

Armstrong, Clarke, and Hill (1987) analyzed total neuron numbers in the anterior principle thalamic nucleus and the medial mamillary body of 17 anthropoid primate species. Their results show that species classified as having uni-male societies have more neurons in the anterior principle thalamic nucleus than do species with multi-male societies. This trend was not present in the medial mamillary body (Armstrong et al., 1987). Volumes, neuronal densities,

neuron numbers, and volumes of neuronal perikarya were measured in the anterior principalis and lateralis dorsalis of the thalamus in humans, chimpanzees, gorillas, and gibbons. Results show that humans have larger nuclei but that these nuclei constitute a similar proportion of the thalamus compared to other hominoids. However, total neuron numbers of these nuclei in humans is much larger than in other hominoids (Armstrong, 1980). It should be noted that both of these studies fall outside the twenty-five-year range set out at the beginning of this paper. They have however been included for their unique and pioneering nature at the time when they were published.

Cytoarchitecture of area 13 in the frontal cortex of humans and apes has been investigated using a Gallyas silver stain. Volume, GLI, relative size of cortical layers, and neuronal counts were obtained for each species. Results reveal that features such as relative size of cortical layers, neuronal densities, and GLI are similar across the species studied. However, there are differences in relative size of area 13 (Semendeferi et al., 1998). Area 13 in humans and bonobos is relatively smaller than in the other species, while in orangutans area 13 is relatively larger (Semendeferi et al., 1998).

Volumes of the amygdala and the basolateral division of the amygdala have been investigated in humans and other apes. In humans the lateral nucleus is larger than expected in an ape of human brain size and occupies most of the basolateral division. In other apes the basal nucleus is the largest nucleus in the basolateral division. The amygdala and basolateral division is smaller in the orangutan than in the African apes and in the gorilla the lateral nucleus is smaller than expected while the basal and accessory basal nuclei are larger than expected (Barger et al., 2007). In addition to volumes, neuronal populations of the amygdala and its subdivisions have also been analyzed in humans and other primate species. The amygdalae of humans,

chimpanzees, bonobos, gorillas, orangutans, and macaques were parcellated into the lateral, basal, accessory basal, and central nuclei based on consistent anatomical landmarks. Neuron counts were then obtained for each nucleus in each species. The data show that the lateral nucleus in humans contains the highest number of neurons, while in apes the basal nucleus has the highest number of neurons. Moreover, the human lateral nucleus had more neurons than expected according to allometric trends (Barger et al., 2012).

An analysis which combined new volumetric data on the whole amygdala, four amygdaloid nuclei, hippocampus, and striatum of humans and apes with previously published volumetric data on the amygdala, orbital and medial frontal cortex, insula, and dorsal frontal cortex found differences between humans and other apes in these regions. The hippocampus, lateral nucleus, and the orbital frontal cortex are larger than expected in humans while the medial and dorsal frontal cortex are smaller than expected. The volume of the striatum is also smaller than expected in comparison to other anthropoid primates (Barger, Hanson, Teffer, Schenker-Ahmed, & Semendeferi, 2014).

Additionally, the volume of the insular cortex and its subregions has been investigated in 30 primate species, including humans and all of the great apes, using Nissl-stained sections. Volumes of the granular, dysgranular, and agranular insular cortices were estimated in each species, and in the humans and great ape species the volume of the frontoinsular (FI) cortex was also estimated. Results indicate that the whole insula scales hyperallometrically relative to brain mass, and the agranular insula scales against total brain mass with even greater positive allometry. Additionally, the absolute volumes of the left and right agranular insula and left FI are differentially expanded in humans compared to chimpanzees (Bauernfeind et al., 2013).

Given the behavioral differences between chimpanzees and bonobos Nissl-stained sections of various brain regions involved in socioemotional processing have been investigated in these species. In this case, the neuropil fraction was calculated for each of these areas (see table). Additionally, in two of these areas, the anterior cingulate cortex (ACC) and the FI, von Economo neurons (VENs), were quantified. Von Economo neurons are a class of neurons thought to be involved in rapid information processing during social situations. Results reveal significantly greater neuropil in the central and accessory basal nuclei of bonobos, and in layers V-VI of the subgenual ACC. There are no differences in the number of VENs between species (Issa et al., 2019).

Immunohistochemistry

Serotonergic innervation of the amygdala has been investigated in chimpanzees and bonobos due to the behavioral differences observed between these species. SERT-ir axon densities were calculated in the whole amygdala, and its lateral, basal, accessory basal, and central nuclei for chimpanzees and bonobos. Results show that bonobos had more than twice the density of SERT-ir axons than chimpanzees. The most pronounced differences in SERT-ir axon densities were found in the basal and central nuclei (Stimpson et al., 2016). Another study of the human amygdala calculated SERT-ir axon density in the lateral, basal, accessory basal, and central nuclei and compared these data to previously published data on chimpanzees and bonobos. Results indicate that SERT-ir axon density is significantly greater in central nucleus compared to the lateral nucleus in humans. The basal, accessory basal, and central nuclei in humans have significantly higher SERT-ir axon density than in chimpanzees, and the accessory

basal and central nuclei in humans have significantly higher SERT-ir axon density than in bonobos (Lew et al., 2019).

Oxytocin (OT) and arginine vasopressin (AVP) influence social cognition in primates Immunohistochemical methods have therefore been used to investigate OT- and AVP-containing fibers in the cortex of humans, chimpanzees, and macaques. In humans and chimpanzees OT-ir fibers were found in the straight gyrus as well as the anterior cingulate gyrus, while no OT-ir fibers were found in the macaque cortex. AVP-ir fibers were found in the anterior cingulate gyrus of all species. In humans AVP-ir fibers were also found in the insular cortex (Rogers et al., 2018).

Neurons immunoreactive for calretinin have been investigated in the anterior cingulate cortex (ACC) of 13 different primate species. Results show that calretinin immunoreactive neurons are rare in orangutans and more common in chimpanzees and gorillas, while humans have the highest numbers of these neurons (Hof et al., 2001).

The results of these studies reveal differences in volumes, neuron numbers, and neuropil space in cortical and subcortical, specifically the amygdala, regions associated with socioemotional processing in humans and apes. Additionally, there are differences in cortical serotonergic innervation along with oxytocin and arginine vasopressin containing fibers in the cortex of different primate species. There are also differences calretinin immunoreactive neurons in the ACC and in serotonergic innervation in the different nuclei of the amygdala.

Explanatory Strategies

This section will cover the three explanatory strategies (mechanical, developmental, and adaptational) in greater detail and revisit the literature reviewed above in the context of these

strategies. However, before moving on to any discussion of explanatory strategies, the principles of evolutionary reconstructions will be briefly reviewed.

Principles of Evolutionary Reconstructions

The Comparative Method

Comparative methods of study are hardly a recent development. Indeed, the use of comparisons to study almost anything (mathematical, philosophical, theological, biological, etc.) can be traced at least back to, if not beyond, ancient Greek thinkers. Moreover, the comparative method has been particularly influential in the biological sciences (Harvey & Pagel, 1991). As the name suggests, the comparative method in biological sciences involves comparisons within, and particularly between, species in order to study basic biological processes (Albert, 2009). Much of Darwin's work in *The Origin of Species* was based upon comparisons of the diverse morphological features and environmental factors he observed. Since Darwin's work, the comparative method has remained a standard technique for addressing evolutionary questions (Harvey & Pagel, 1991). Comparisons between species "allow for the systematic study of organismal design," (Albert, 2009). Characteristics of different species can then be understood through application of concepts such as homology, similarities do to common ancestry, homoplasy (including convergence, parallelism, and reversal), other forms of phenotypic similarity, and phylogenetic trees. In short, the comparative method is quite a useful tool in evolutionary biology generally and, of particular importance for this paper, evolutionary neurobiology and can yield a great deal of information. However, these comparisons and interpretations must be carefully made in order to be maximally useful (Albert, 2009).

Phylogenetic Reconstruction

Comparative analyses begin with an assumed hypothesis about the genealogical relatedness of the taxa of interest (Albert, 2009). Therefore, implicit in the methods for studying character evolution is a tree-shaped, branching diagram (Albert, 2009). Indeed, Darwin himself included a diagram which very much resembled a phylogenetic tree in his chapter on natural selection in *The Origin of Species*. Darwin's version naturally did not employ the same statistical methods which are used today, but its inclusion indicates how deeply embedded this sort of model is in evolutionary thought (Darwin, 2009). Today there are various names for this sort of diagram, including dendrograms, cladograms, phenograms, or trees, depending upon the methods employed in construction and the information conveyed. Phylogenetic methods can then be used to understand character states at different points, often hypothesized speciation events, on the tree (Albert, 2009).

There are a number of different phylogenetic methods which can be employed in evolutionary reconstructions some of which will be touched upon here. One such method involves the principle of parsimony. The principle of parsimony is frequently used in the natural sciences to choose from multiple hypotheses. The idea is that the number of entities used to explain anything should not be increased beyond what it necessary. Essentially, simple hypotheses are given preference over more complicated ones. In the context of phylogenies, maximum parsimony is used to minimize the number of evolutionary steps required to explain a given set of data. There are two kinds of maximum parsimony which are typically employed in tracing the lineage of continuous traits, linear parsimony and squared change parsimony. Linear parsimony minimizes the total amount of evolution. Linear parsimony also allows for the accurate reconstruction of discontinuous events or large changes in trait values. Squared change

parsimony minimizes squared change along each branch of the entire tree at once. Maximum likelihood and Bayesian analysis are both model based approaches commonly used in the analysis of gene sequence data. Each of the methods mentioned here has its strengths and weaknesses and the usefulness of each depends upon the circumstances under which they are applied (Albert, 2009). However, regardless of which method is used careful consideration goes into the evolutionary reconstruction of particular character traits.

It is worth noting here the transition from the *scala naturae*, to the phylogenetic scale, and finally to the phylogenetic trees discussed above. The *scala naturae* is an old idea which places species in a given order according to their presumed level of perfection. This sort of scale of perfection then gave way to the phylogenetic scale. Again, this particular method of understanding species relatedness organized different species onto a scale. As species evolve, they ascend to a higher wrung on the scale. The problem with this is that the single scale model fails to capture the complexity of evolution. That is, ranking on a scale will change depending upon the traits being considered, and complexity tends to both increase and decrease over the course of evolution. The metaphor of a bush, rather than a tree, has therefore been proposed to combat the strict linear organization necessitated by thinking of evolution in terms of a scale (Striedter, 2009). However, while the influence our use of language and metaphor has over our thinking is an interesting thing to consider, the important point is that there must always be a balance between the simplifying assumptions necessary for evolutionary reconstructions and the complexity of evolutionary processes. Indeed, current phylogenetic methods no longer operate under the assumptions imposed by a scale. Instead, each species is understood as one specialized endpoint of evolution (Preuss, 2009).

Three Explanatory Strategies

As with any scientific endeavor, interpretation of data is an important part of comparative neuroanatomical studies. That is, the data must be explained, not just catalogued. In comparative studies of the brain species similarities are explained as either the result of homology or analogy. In other words, similarities observed between species arise because the last common ancestor of the species in question also had the neural trait being observed, or they arise as the result of convergent evolution. It is slightly more difficult to explain species differences because causal explanations of how and why particular neural characteristics evolved must be provided. One step removed from these causal explanations is the question of what strategies can be used to make them. Various strategies have been proposed to explain species difference (Amundson, 1994; Gould & Lewontin, 1979; Maynard Smith et al., 1985) and Striedter (2005) has synthesized these into three main strategies. These are mechanical, developmental, and adaptational explanations (Striedter, 2005).

Mechanical Explanations

The first explanatory strategy to be discussed is mechanical explanations of species difference. This rests on constraints imposed on evolution by certain mechanical factors (Gould & Lewontin, 1979; Striedter, 2005). That is, differences in neural characteristics between species are explained in terms of the mechanical traits that "forced" their evolution (Gould & Lewontin, 1979; Striedter, 2005).

An example of this kind of explanation is the evolution of highly folded neocortices (Zilles, Armstrong, Moser, Schleicher, & Stephan, 1989).The neocortex of very small primates, such as galagoes and marmosets, does not exhibit a high degree of folding. However, when

absolute brain size crosses the 5-10g threshold the neocortex becomes increasingly folded (Striedter, 2005). An explanation of this phenomenon is that as absolute brain size increases, thickness of the neocortex remains relatively constant while thickness of the telencephalic base increases. In other words, the surface area of the neocortex expands more quickly than the base it is attached to. When growth of the outer layers exceeds growth of the inner layers the result is a more gyrified brain (Zilles et al., 1989). In this case, highly folded cortices evolved as a result of spatial constraints imposed on an expanding neocortex. Moreover, this trend of highly folded cortices in large brained members of a lineage is also observed in a number of other mammalian species, not just primate species. This strengthens the hypothesis that more highly folded cortices appear after the 5-10g absolute brain size (depending upon species) threshold has been crossed (Striedter, 2005). Additionally, Van Essen (1997) has also explained species-specific folding patterns of the cerebral and cerebellar cortices in mammalian species in terms of mechanical tension along axons.

Developmental Explanations

The next strategy to be discussed is developmental explanations. This strategy focuses on brain development in the evolution of particular neural characteristics (Amundson, 1994; Maynard Smith et al., 1985; Striedter, 2005). In this case, the evolution of particular neural characteristics is explained as the result of some constraining rule of brain development (Amundson, 1994; Maynard Smith et al., 1985; Striedter, 2005).

A good example of this kind of explanation is the “later equals larger” model. The “later equals larger” model seeks to explain correlations observed between absolute brain size, the relative size of various brain regions, and when those regions appear in development using data

collected from 131 mammalian species. Essentially this model proposes that as brain size increases the order in which different brain regions appear does not change. Schedules of neurogenesis are either squeezed or stretched, not rearranged. Large mammals therefore have longer periods of brain development than smaller mammals, however the schedule of neurogenesis is the same. The implication of this conserved schedule of neurogenesis is that the later a given region of the brain appears in development, the larger it will become as absolute brain size increases (B. L. Finlay & Darlington, 1995).

Adaptational Explanations

The final strategy to be discussed is adaptational explanations. In this case the strategy is to ask what a particular neural characteristic may have been selected for (Amundson, 1994; Gould & Lewontin, 1979; Striedter, 2005). It is fairly straightforward to understand this particular explanatory strategy. However it is not without its difficulties, particularly in the realm of brain evolution (Amundson, 1994; Gould & Lewontin, 1979; Striedter, 2005).

The relationship between brain anatomy and physiology to animal behavior is still incomplete. It is therefore difficult to explain the appearance of a particular neural characteristic based upon its adaptive significance. Moreover, it is difficult to test such hypotheses because it is difficult, if not impossible, to manipulate neural characteristics and observe the effect of this manipulation on individual fitness. This sort of explanation is therefore easier to discuss than to demonstrate. It is possible to reduce uncertainty about adaptational explanations by demonstrating that a particular neural characteristic has evolved repeatedly in several different lineages and is consistently associated with a particular behavior. If this is the case, then the feature in question is more likely to have evolved as an adaptation for that particular behavior.

However, even this is insufficient since correlations alone cannot be used to prove a causal link. Even so, in the event that such correlations can be combined with functional data this becomes strong evidence that a neural character evolved as an adaptation for a behavior (Striedter, 2005).

Application to Human/Ape Comparative Literature

The synthesis proposed by Striedter creates a very neat and comprehensive division of explanatory strategies. However, Striedter's synthesis, and some of the original sources from which it was derived, are not specifically focused on human/ape comparisons (Amundson, 1994; B. L. Finlay, Darlington, & Nicastro, 2001; Gould & Lewontin, 1979; Maynard Smith et al., 1985; Striedter, 2005). The question becomes whether, and how, this model can be employed in the literature which deals specifically with comparisons between humans and apes? It seems reasonable to assert that these three explanatory strategies are useful in comparative studies between primates given that they are rather broad, comprehensive categories. However, just what these categories mean for, how they apply to, and how they intersect in human/ape comparative neuroanatomical work requires a more in-depth discussion. The following section will therefore take another look at the human and ape comparative literature from the last twenty-five years in relation to of these three strategies.

Mechanical Explanations

Mechanical explanations are tightly linked to cortical folding (Van Essen, 1997; Zilles et al., 1989) and therefore to mammalian species generally, and primate species in particular. However, very few of the papers reviewed here explicitly employ mechanical explanations in their interpretations of species differences.

Macro: Executive Functioning. A possible increase in gyral white matter volumes in humans, and a larger ratio of gyral white matter to cortex in the two *Pan* species compared with *Gorilla* and *Pongo* was observed in the investigation of frontal and temporal lobe volumes by Schenker et al. (2005). The possible increase in gyral white matter volume is understood to reflect a possible increase in connectivity between neighboring cortical areas which may be related to human cognitive function, though no claim is made as to what these functions might be. It is however suggested that the increase in gyral white matter seen in humans may be related to increased gyrification in the human cortex. Likewise, it is suggested that the increase in the gyral white matter of the two *Pan* species may be related to increased gyrification (Schenker et al., 2005).

The studies investigating cortical thickness, gyrification, and white matter volume between humans and chimpanzees revealed that humans had a greater degree of gyrification and thinner cortex than chimpanzees, particularly in the frontal lobe (Hopkins & Avants, 2013; Hopkins et al., 2017). Additionally, frontal lobe white matter volumes were higher in humans than in chimpanzees. The authors suggest this increased gyrification in humans may be the result of the increased white matter also found in humans. Moreover, the thinner cortex may also be explained as a result of increasing white matter volume (Hopkins et al., 2017).

Macro: Speech and Language. The analysis of white matter connectivity in humans and chimpanzees revealed particular links in humans between multimodal areas of the temporal, lateral parietal, and inferior frontal cortices, including white matter tracts important in language processing. Furthermore, network analysis demonstrated that these connections are responsible

for particularly high contributions to global network integration in the human brain. A couple of explanations for the differences observed in white matter connectivity between humans and chimpanzees are proposed, one such explanation being that changes in connectivity are the result of brain expansion (Ardesch et al., 2019).
(See also, Hopkins and Avants 2013).

Macro: Whole Brain. Chen et al.'s (2013) investigation of the relationship between gyral folding and structural connection patterns in humans, chimpanzees, and macaques revealed that structural fiber connection patterns closely follow gyral folding patterns in the direction tangent to the cortical sphere in all species studied, despite the increase in complexity and variability of folding and fiber patterns in each species. They suggest that an axonal fiber pushing mechanism is integral to gyral morphology. In other words, the gyral patterns which emerged over the course of primate evolution are the result of a mechanical constraint imposed by axonal fiber pushing (Chen et al., 2013). Likewise, the paper by Li et al. (2017) on gyral folding patterns, which will be discussed in more detail in regard to developmental explanations, also notes the need for a mechanically based explanation of the observed species differences although no such explanations is actually proposed.

Micro: Future Planning. Finally, the volumetric analysis of frontal and non-frontal white and grey matter in 18 anthropoid species revealed that the hyperscalling of the neocortex and frontal lobe to the rest of the brain is largely due to changes in frontal white matter. Moreover, changes in frontal lobe white matter are linked to changes in the rest of the brain and basal ganglia (Smaers et al., 2010).

In all of these cases the differences observed between species are explained in terms of the constraining effects imposed by specific mechanical considerations. However, it is worth noting that all of these cases also leave open the possibility of further explanation through the application of other explanatory strategies.

Developmental

Developmental explanations of species differences are certainly employed in the comparative primate literature. However, while these explanations do make use of the constraining effects of development on evolution, they also implicate alterations of the developmental schedule in the evolution of particular neural characteristics.

Macro: Executive Functioning. Sakai et al.'s (2013) investigation of the developmental pattern of cerebral tissue in humans and chimpanzees indicated that both humans and chimpanzee display a protracted period of development during prepuberty, but humans also displayed a rapid increase of total cerebral volume during early infancy which was not observed in chimpanzees. This rapid increase in humans is driven largely by a dramatic increase in white matter volume. Based on these findings Sakai et al. (2013) suggest that developmental changes, driven by the elaboration of neuronal connections, may have promoted the evolutionary enlargement of the human brain (Sakai et al., 2013). Similarly, the investigation of the development of prefrontal white matter in humans and chimpanzees revealed that prefrontal white matter volume in chimpanzees, like humans, has not reached adult values during prepuberty. However, the rate of prefrontal white matter volume increase during infancy is slower in chimpanzees than in humans. It is suggested that the extension of the period of

prefrontal connection maturation in chimpanzees and humans is responsible for the expansion of these regions in these two species. However, it is also suggested that the lineage leading to humans has undergone evolutionary modification leading to a period of rapid development during infancy which facilitates the development of complex social interactions (Sakai et al., 2011). In both of these cases expansion of the developmental period is used to explain the evolutionary expansion of frontal lobe regions in the species studies. However, changes to the developmental schedule are also implicated in human-specific differences in frontal lobe regions. Additionally, Aldridge's (2011). whole brain analysis of humans and apes revealed patterns of morphology that were consistently different between humans and all ape species, as well as patterns that differed among ape species. These differences in morphology between species are said to reflect changes in the development of each species (Aldridge, 2011).

Macro: Whole Brain. Li et al.'s (2017) analysis of gyral folding patterns in humans, chimpanzees, and macaques identified 6 common three-hinge gyral folds across species, 6 that were unique to chimpanzees and 14 unique to humans. The 6 common three-hinge folds are located around the central sulcus. It is hypothesized that the convolution process of these three-hinges follow similar rules across species due to the timing of the emergence of the central sulcus during development and the shape of the brain in humans, chimpanzees, and macaques during this period (Li et al., 2017). This is in line with the idea that aspects of development shape the evolution of certain neural characteristics. It is however further suggested that a deeper understanding of both developmental and mechanical influences is needed to understand the gyral folding patterns of these species (Li et al., 2017).

In all of these cases species differences are explained in terms of the constraining effects of brain development on the evolution of a particular characteristic. However, in some of these cases an alteration in the developmental schedule is also implicated in the evolution of the neural characteristic in question.

Micro: Future Planning. A similar pattern can be observed in the microstructural literature. The study of myelination in the human and chimpanzee cortex revealed that density of myelinated axons in chimpanzees increased steadily throughout development with adult-like levels being reached around the time of sexual maturity. However, humans displayed a slower development through childhood with a delayed period of maturation that extends beyond late adolescence. The authors suggest these differences may be reflect an evolutionary modification of the developmental schedule in humans (Miller et al., 2012). The analysis of the development of spatial organization of neurons in the neocortex of humans and chimpanzees demonstrated that in both humans and chimpanzees HSD in BA 10 was significantly higher in postweaning specimens, while no significant age-related differences were found in the other cortical areas. It is noted that the late developing regions are those which have expanded most during the course of evolution and suggested that protracted development allows for greater elaboration of dendritic arbors in these late developing regions (Teffer et al., 2013).

Micro: Speech and Language. The analysis of linear organization of area Tpt in humans, chimpanzees, and macaques showed that the arrangement of cells in layers III and, to a lesser extent, V closely resemble the fetal template in all species, while arrangement of cells in layers II and IV diverge from this template. Cell density is less in the species with larger brains and this

difference is largely due to an increase in distance between cell columns. Additionally, horizontal distance is widest in humans and this distance in most pronounced in layer II and least pronounced in layer III (Buxhoeveden et al., 1996). The analysis of cellular organization in Broca's area in humans, apes, and macaques revealed that humans had the largest neuropil volume, the great apes had lower neuropil volume, and macaques had the lowest neuropil volume. This suggests more space for connections in human BA 44 and 45 than in the other primate species. The differences in neuropil fraction in Broca's area in humans may be due to differences in the developmental trajectory of this region (Palomero-Gallagher & Zilles, 2019).

Micro: Learning and Memory. Raghanti et al.'s (2011) analysis of cholinergic innervation in the nucleus basalis of Meynert in anthropoid primates showed that changes in the cholinergic system among primate species involve axon terminations in the neocortex rather than in subcortical neurons providing innervation because there is not an increase in subcortical neurons providing cortical innervation. They suggest that this may be the result of developmental constraints on the basal forebrain which result from the large neocortex found in primates (Raghanti et al., 2011).

Once again, species differences are explained in terms of the constraining effects of brain development on the evolution of a particular characteristic. However, in some of these cases, an alteration in the developmental schedule is also implicated in the evolution of the neural characteristic in question. This perhaps results from the fact that the forces underlying these explanatory strategies do not operate independently and mechanical or selective pressure may alter development in different species.

Adaptational

Adaptational strategies, as laid out above, explain neuroanatomical differences between species as the result of selection for a particular behavior (Amundson, 1994; Gould & Lewontin, 1979; Striedter, 2005). This particular strategy has however been criticized for two main reasons. The first is that is that the relationship between anatomy and function is not sufficiently well known to make such assertions. The second is that this kind of strategy tends to focus on solely on the adaptive value of a particular behavior in the evolution of a particular neural characteristic to the exclusion of other influential factors (i.e. mechanical or developmental constraints). The literature from the last twenty-five years discussed here therefore uses what is essentially the inverse of adaptational strategies described above. That is, the focus is shifted to the appearance of a particular neural characteristic in a given species and the behavioral adaptations which may be related to this anatomical difference are merely suggested. It is left open whether these behavioral adaptations may drive the evolution of a particular neural character, or whether they may be a consequence of that evolution. This model allows for explanations which can be more readily supported by data, and which do not focus on the adaptive value of particular behaviors to the exclusion of other factors.

Macro: Executive Functioning. In all of the cases discussed in this paper emphasis is on the presence of a particular neural characteristic rather than the selection for a behavior. The volumetric estimates of the frontal lobe, its subsectors, and the temporal lobe in humans and apes obtained by Schenker et al. (2005) revealed remarkable homogeneity between humans and apes. Even so, there are some notable differences between species. One such difference is the relatively small size of the orbital sector in orangutans. Two possible explanations for the size of

the orbital sector are proposed. This first is that some of the cortical areas included in the orbital sector of the other apes have been moved laterally in the orangutan, thereby decreasing the size of the orbital sector. The second is that the decreased orbital sector reflects differences in evolutionary pressures related to social interactions (Schenker et al., 2005). The analysis of prefrontal grey matter in humans, chimpanzees, and macaques revealed that the proportion of grey matter occupied by the prefrontal cortex in humans is 1.2-fold greater than in chimpanzees and 1.9-fold greater than in macaques. Additionally, the proportion of white matter underlying the prefrontal cortex is 1.7-fold greater in humans than chimpanzees and 2.4-fold greater in humans than macaques. These differences may be related to distinctively human behavioral and cognitive capacities (Donahue et al., 2018). MRI scans of chimpanzee brains obtained by Hopkins and Avants (2013) revealed significant regional variation in cortical thickness. In particular, primary motor and sensory areas showed lower values compared to association cortex. Furthermore, chimpanzees displayed rightward asymmetries in cortical thickness and leftward asymmetries in white matter volume. Finally, cortical thickness was found to be negatively correlated with white matter volume. It is suggested that asymmetry was present in the last common ancestor between humans and chimpanzees and that patterns of asymmetry in these species may reflect unique ecological pressures (Hopkins & Avants, 2013).

Macro: Speech and Language. The volumetric analysis of the temporal lobe, superior temporal gyri, and temporal lobe white matter volume in 44 anthropoid primate species determined that the volume of the human temporal lobe is larger than expected. Moreover, human temporal lobe white matter volume is larger than predicted for brain size and predicted for temporal lobe volume. It is suggested that these differences may reflect adaptations

supporting species-specific communication in the species studied (Rilling & Seligman, 2002). Furthermore, investigation of the arcuate fasciculus in humans, chimpanzees, and macaques revealed a prominent temporal lobe projection in humans which was not present in either of the other two species studied. The authors suggest that expansion in certain cortical areas in the human brain resulted in new connections related to the evolution of language (Rilling et al., 2007).

The investigation of the volumes of selected brain regions in chimpanzees and bonobos revealed that the chimpanzee hippocampus was borderline significantly larger than in bonobos. In bonobos there were greater leftward asymmetries in the striatum and motor-hand area, while in the inferior frontal gyrus and planum temporale there were no significant differences between species. It is suggested that the hippocampal differences between species may reflect differences in the size of home ranges. Chimpanzees have relatively larger home ranges which might place greater demand on chimpanzee spatial memory. It is further suggested that the greater leftward asymmetry in the bonobo striatum may reflect greater oro-facial motor control in bonobos (Hopkins et al., 2009).

Finally, the whole brain analysis of humans and apes revealed patterns of morphology that were consistently different between humans and all ape species, as well as patterns that differed among ape species. It is suggested that some of the most notable differences in the pattern of morphology observed in humans may reflect adaptations for language and an increased importance of the amygdala in human brain evolution (Aldridge, 2011).
(See also, Hopkins and Avants 2013)

Macro: Learning and Memory. The study of SLF connectivity and mirror self-recognition in chimpanzees showed that successful self-recognition was associated with rightward asymmetry in the white matter of SLF II and III, as well as the grey matter termination of SLF III Additionally, it was noted that chimpanzees with more human-like SLF connectivity exhibited more human-like behaviors. It is suggested that mirror self-recognition may be linked to other behaviors which involve similar processes including, language, tool use, and social learning. These functions involve similar overlapping networks and may have coevolved in a mutually reinforcing way (Hecht et al., 2017). (See also, Hopkins, et al. 2009)

Macro: Socioemotional Processing. The analysis of the neural systems underlying cognition in chimpanzees and bonobos showed that bonobos have more grey matter in brain areas important in perceiving distress, as well as a larger path linking the amygdala and ventral anterior cingulate cortex. This pathway is implicated in top-down control of aggressive impulses, as well as bottom-up biases against harming others. It is suggested that these differences support increased empathetic sensitivity in bonobos in addition to behaviors which dissipate stress (Rilling et al., 2012).

In all of the above cases species differences are explained by highlighting the appearance of a particular neural characteristic in the lineage leading to the human or ape species being studied, rather than the selection of a particular behavior in the lineage of that species. This kind of explanation is more readily supported by available evidence and avoids focusing on the adaptive significance of particular behaviors to the exclusion of other factors.

Micro: Future Planning. The same holds true for studies conducted at the microstructural level. The study of area 10 in humans and apes revealed that area 10 in humans is larger relative to the rest of the brain relative to other apes. Additionally, there is more space available for connections in area 10, specifically in the supragranular layers. The specialization of area 10 in the human brain suggests functions associated with this area, particularly planning of future actions and undertaking of initiatives, became particularly important during human evolution (Semendeferi et al., 2001). Another study of the frontal cortex in humans and apes revealed different scaling coefficients in the right versus left prefrontal region suggesting that left hemispheric prefrontal hyperscaling is a primary factor underlying primate brain evolution with humans at the extreme end of this trend. This structural lateralization is said to reflect a neural adaptive shift which underlie a cognitive grade shift between great apes and other primate species (Smaers et al., 2011). The investigation of spatial organization of neurons in area 10 in humans and apes indicate that the horizontal spacing distance of neurons in area 10 is greater in humans than other apes. Moreover, grey-level ratio is correspondingly lower in area 10 in humans compared to other apes. The more widely spaced neurons observed in humans may be related to behavioral differences in associative functions, particularly executive functions (Semendeferi et al., 2011). The investigation of neuropil distribution in the cerebral cortex of humans and chimpanzees revealed that BA 10 and area FI in humans have a significantly higher neuropil fraction than other areas. This was not the case in chimpanzees, although BA 41/42 in chimpanzees did display a lower neuropil fraction than other areas. These findings support the conclusion that evolution of the human prefrontal cortex was accompanied by enhanced connectivity, which may support an increase in executive cognitive functions (Spocter et al., 2012).

The comparison of dendritic morphology in pyramidal neurons in the chimpanzee neocortex compared to those in humans revealed greater dendritic complexity in BA 10 of both humans and chimpanzees that was not present in other cortical areas. However, in humans pyramidal neurons displayed longer, more complex branching in all cortical areas examined. These results also support the conclusion that human prefrontal cortical evolution is supported by increased potential for connectivity which may underlie executive cognitive function (Bianchi, Stimpson, Bauernfeind, et al., 2013). Similarly, the investigation of synaptogenesis and development of dendritic morphology in humans and chimpanzees showed that synaptogenesis occurs at the same time across cortical regions and there is a peak of synapse density during the juvenile period. Additionally, pyramidal neurons in the prefrontal cortex develop later than those in other cortical areas This is consistent with similar data collected in humans. This delayed development may reflect adaptations for greater neuronal plasticity which underlies experience dependent behaviors (Bianchi, Stimpson, Duka, et al., 2013).

Micro: Speech and Language. Buxhoeveden et al.'s (2001) analysis of minicolumnar organization of the planum temporale in humans, chimpanzees, and macaques reveals wider minicolumns and more neuropil space in the left hemisphere in humans. The investigation of minicolumnar organization of Broca's area in humans and great apes revealed that there were no population-level asymmetries in HSD or GLI. However, GLI was higher in humans than in the great apes. HSD in humans was also greater in terms of absolute size, but smaller than the great apes relative to brain size. These results suggest an increase in microcircuitry in these regions in humans which may be related to hierarchical processing abilities (Schenker et al., 2008). The

analysis of Wernicke's area in humans and chimpanzees revealed population-level leftward asymmetry in total neuron number, as well as a volumetric asymmetry approaching significance. Moreover, asymmetry in neuron numbers in area Tpt, a component of Wernicke's area, was positively correlated with an asymmetry in neuron numbers in BA 45, a component of Broca's area. These results indicate that a leftward asymmetry in Wernicke's area appeared before the split with chimpanzees and may reflect an adaptation for conveying communicative information to the action planning system, rather than an adaptation for language (Spocter et al., 2010).

The analysis of dopaminergic innervation in the basal ganglia of humans and other primates indicated that there is an increase of dopaminergic innervation in the medial caudate nucleus in humans compared to the other species studied. Moreover, there was no change in dopaminergic innervation in chimpanzees that used socially learned attention-getting sounds compared to those that did not. This increase in dopaminergic innervation in the medial caudate may be related to the evolution of speech and language in humans (Raghanti et al., 2016).

Micro: Learning and Memory. The investigation of serotonergic innervation in the cortex of humans, chimpanzees, and macaques revealed no quantitative increase in serotonergic innervation in the human frontal cortex compared to chimpanzees and macaques. However, humans and chimpanzees displayed greater SERT-ir axon densities relative to neuron densities in layers V/VI in areas 9 and 32. Moreover, axon coils were observed in humans and chimpanzees, but not in macaques. These findings indicate significant reorganization of the cortical serotonergic transmission in humans and chimpanzees. This reorganization may reflect adaptations for a greater capacity for cortical plasticity which may in turn support a greater capacity for learning and behavioral flexibility in these species (Raghanti et al., 2008d).

The study of cortical dopaminergic innervation in humans, chimpanzees and macaques revealed a sublaminar pattern of innervation in layer I of areas 9 and 32 in humans which was not present in the other species. Additionally, both humans and chimpanzees displayed an increase in dopaminergic innervation in layers III, V/VI in areas 9 and 32 which was not present in macaques. Moreover, axon coils, which may be related to cortical plasticity events, were observed in humans and chimpanzees, but not in macaques. These results suggest significant modification in dopaminergic innervation in the cortex of apes, and further modification in the human cortex. This reorganization too may reflect adaptations for a greater capacity for cortical plasticity which may in turn support a greater capacity for learning and behavioral flexibility (Raghanti et al., 2008b). The related analysis of dopaminergic innervation in the prefrontal cortex of anthropoid primates revealed TH-ir neurons in layers V/VI and the white matter below in humans, Old World monkeys, and siamangs. TH-ir neurons were also observed occasionally in humans, the siamang, and some of the monkey species. TH-ir cells were noticeably absent in the cortex of the great ape species studied. Additionally, humans and the monkey species both showed a bilaminar pattern of TH-ir axon distribution in the prefrontal regions. Layers I/II and V/VI in humans and monkeys had the highest TH-ir axon density. In the great apes TH-ir axons were most dense in layer III (Raghanti et al., 2009).

The investigation of cholinergic innervation of the basal ganglia in anthropoid primates revealed that humans and great apes have a preponderance if multipolar ChAT-ir interneurons in the caudate nucleus and putamen, while monkeys displayed a heterogenous mix of multi-, bi-, and unipolar interneurons. Differences in ChAT-ir axon and interneuron densities were observed in the dorsal caudate, putamen, and globus pallidus, but these differences were not associated

with the phylogenetic structure of the species studied. In combination with previously published data, these results revealed a unique pattern of innervation in humans. These results may reflect adaptations for greater plasticity (Stephenson et al., 2017). The analysis of cholinergic innervation in the frontal cortex of humans, chimpanzees, and macaques revealed clusters of cholinergic fibers in humans and chimpanzees but not in macaques. These finding suggest alterations in cholinergic innervation of the human and chimpanzee cortex. These alterations may reflect adaptations for cortical plasticity underlying increased capacity for learning and memory (Raghanti et al., 2008a).

Micro: Socioemotional Processing. The analysis of the anterior principalis and lateralis dorsalis of the thalamus in humans, chimpanzees, gorillas, and gibbons demonstrate that these nuclei are absolutely larger in humans, but that they constitute a similar proportion of the thalamus compared to other hominoids. However, total neuron numbers of these nuclei in humans is much larger than in other hominoids (Armstrong, 1980). Additionally, the investigation of the anterior principle thalamic nucleus and the medial mamillary body of 17 anthropoid primate species reveals that species classified as having uni-male societies have more neurons in the anterior principle thalamic nucleus than do species with multi-male societies (Armstrong et al., 1987).

The investigation of area 13 in humans and apes revealed that features such as relative size of cortical layers, neuronal densities, and GLI are similar across the species studied. However, there are differences in relative size of area 13. Area 13 in humans and bonobos is relatively smaller than in the other species, while in orangutans area 13 is relatively larger. These differences may be related to differences in social systems or processing of emotional states

(Semendeferi et al., 1998). The study investigating the insular cortex in humans and apes revealed that the whole insula scales hyperallometrically relative to brain mass, and the agranular insula scales against total brain mass with even greater positive allometry. Additionally, the absolute volumes of the left and right agranular insula and left FI are differentially expanded in humans compared to chimpanzees. These difference may be related to the evolution of complex social interactions, such as empathy and cooperation, which have amplified in the human lineage (Bauernfeind et al., 2013). The analysis of oxytocin- and arginine vasopressin-containing fibers in the cortex of humans, chimpanzees, and macaques revealed OT-ir fibers were found in the straight gyrus as well as the anterior cingulate gyrus in humans and chimpanzees, while no OT-ir fibers were found in the macaque cortex. AVP-ir fibers were found in the anterior cingulate gyrus of all species. In humans AVP-ir fibers were also found in the insular cortex. OT in the straight and anterior cingulate gyri in humans and chimpanzees may play a conserved role in detecting and responding to the emotional states of others, while AVP in the insular cortex may be related to empathetic behaviors in humans (Rogers et al., 2018).

Volumetric analyses of the amygdala and its basolateral division in humans and apes show that the human lateral nucleus is larger than expected in an ape of human brain size and occupies most of the basolateral division. In other apes the basal nucleus is the largest nucleus in the basolateral division. The amygdala and basolateral division are smaller in the orangutan than in the African apes and in the gorilla the lateral nucleus is smaller than expected while the basal and accessory basal nuclei are larger than expected. These finding may reflect differences in social behavior (Barger et al., 2007). Another analysis of the amygdala in humans and apes revealed that the lateral nucleus in humans contains the highest number of neurons, while in apes the basal nucleus has the highest number of neurons. Moreover, the human lateral nucleus had

more neurons than expected according to allometric trends. This increase in the lateral nucleus may reflect a need to process increased cortical inputs and emotional elements related to human communicative repertoires and social networks (Barger et al., 2012). The investigation of serotonergic innervation of the amygdala in chimpanzees and bonobos revealed that bonobos had more than twice the density of SERT-ir axons than chimpanzees. The most pronounced differences in SERT-ir axon densities were found in the basal and central nuclei. These differences may be related to the evolution of the different behaviors observed in these species (Stimpson et al., 2016). The investigation of the human amygdala by Lew et al. (2019) revealed that SERT-ir axon density is significantly greater in central nucleus compared to the lateral nucleus in humans. The basal, accessory basal, and central nuclei in humans had significantly higher SERT-ir axon density than in chimpanzees, and the accessory basal and central nuclei in humans had significantly higher SERT-ir axon density than in bonobos. These results complement the redistribution of neurons that has been observed in the human amygdala and suggest that differential serotonergic innervation may be related to differences in social behavior (Lew et al., 2019).

The volumetric analysis of multiple limbic structures in humans and apes shows that the hippocampus, lateral nucleus of the amygdala, and the orbital frontal cortex are larger than expected in humans while the medial and dorsal frontal cortex are smaller than expected The volume of the striatum is also smaller than expected in comparison to other anthropoid primates (Barger et al., 2014). The investigation of socioemotional circuits in chimpanzees and bonobos revealed significantly greater neuropil in the central and accessory basal nuclei of bonobos, and in layers V-VI of the subgenual ACC. There were no differences revealed in the number of VENs between species. These results may be related to the behavioral differences observed

between these species (Issa et al., 2019). Quantification of calretinin-immunoreactive neurons in the anterior cingulate cortex of several 13 primate species shows that calretinin-immunoreactive neurons are rare in orangutans and more common in chimpanzees and gorillas, while humans have the highest numbers of these neurons. These results suggest unusual and rapid adaptive pressure in the anterior cingulate cortex of Old World primates, which may be related to cognitive processes related to emotional processing (Hof et al., 2001).

Once again, species differences are explained by highlighting appearance of a particular neural characteristic over the selection of a particular behavior which led to the evolution of the neural characteristic in question. This kind of explanation is more readily supported by available evidence and avoids focusing on the adaptive significance of particular behaviors to the exclusion of other factors. Indeed, this is evidenced by the fact that some of the studies discussed in this section also employed other explanatory strategies.

Conclusions

There is a great deal of interest in understanding cognitive and behavioral differences between humans and apes (and other primates more generally). One way to do this, is to investigate the evolution of the neurological substrates underlying these cognitive and behavioral differences in humans and apes. Comparative neuroanatomy and the application of phylogenetic principles can be used to reconstruct human brain evolution. Approaches for studying primate brain anatomy can be divided into those which are applicable at the macrostructural level and those applicable at the microstructural level. Macrostructural approaches involve the use of imaging technologies, while microstructural approaches involve the use of different staining techniques. This paper reviewed findings from human/ape comparative neuroanatomy from the

last twenty-five years at both the macro- and micro structural levels. These findings were then discussed in the context of strategies which have been employed to explain species differences more generally in comparative studies. These strategies are mechanical, developmental, and adaptational explanations. Mechanical explanations understand species difference in terms of the constraining of certain mechanical considerations (Gould & Lewontin, 1979; Striedter, 2005). Developmental explanations appeal to the constraining effect certain rules of neural development may have had on the evolution of the primate brain (Amundson, 1994; Gould & Lewontin, 1979; Maynard Smith et al., 1985; Striedter, 2005). Finally, adaptational explanations attribute species difference to selection for a particular behavior which results in the evolution of the neural characteristic in question (Amundson, 1994; Gould & Lewontin, 1979; Striedter, 2005).

These strategies are very clearly applicable to the human/ape comparative literature though not in the cut and dried way in which they were first presented. Instances of mechanical explanations are fairly straightforward, although somewhat infrequent. Developmental explanations are more common however, in addition to the constraining effects of development on the evolution of the brain, these explanations also explore the effect alterations to the developmental schedule may have had on brain evolution. Adaptational explanations have historically been employed with some frequency, particularly as regards brain regions related to language processing (Falk, 1980; Hewes et al., 1973; Parker & R., 1979). However, these purely adaptational explanations have been criticized for their reliance on plausibility rather than evidence and their failure to consider or account for other factors (i.e. mechanical or developmental constraints) in the evolution of particular neural characteristic (Gould & Lewontin, 1979). Within the recent human/ape comparative literature this explanatory problem seems to be combated by focusing instead on appearance of a particular neural characteristic and

suggesting behavioral adaptations which may be related to this anatomical difference. This model allows for explanations which can be more readily supported by data, and which do not focus on the adaptive significance of particular behaviors to the exclusion of other factors.

It should further be noted that the literature discussed in this paper reflects a need to employ more than one strategy at a time in order to provide a thorough explanations of the differences observed between species. Indeed, several of the papers discussed here do just that (Aldridge, 2011; Hopkins & Avants, 2013; Li et al., 2017; Schenker et al., 2005). Moreover, those papers which do not explicitly appeal to more than one explanatory strategy leave open the possibility that one can be applied in the future. This is perhaps indicative of the fact that, while this tripartite division of explanatory strategies is a useful tool for framing and understanding our interpretations of species difference, it is not reflective of the way the processes underlying these strategies actually act on a given species

References

Albert, J. S. (2009). Phylogenetic character reconstruction. In J. H. Kass, G. F. Striedter, J. L. Rubenstien, T. H. Bullock, L. Krubitzer, & T. Preuss (Eds.), *Evolutionary Neuroscience* (pp. 19-31). Oxford, UK: Academic Press.

Aldridge, K. (2011). Patterns of differences in brain morphology in humans as compared to extant apes. *Journal of Human Evolution, 60*(1), 94-105. doi:10.1016/j.jhevol.2010.09.007

Amundson, R. (1994). Two concepts of constraint: adaptationism and the challenge from developmental biology. *Philosophy of Science, 61*(4), 556-578.

Ardesch, D. J., Scholtens, L. H., Li, L., Preuss, T. M., Rilling, J. K., & van den Heuvel, M. P. (2019). Evolutionary expansion of connectivity between multimodal association areas in the human brain compared with chimpanzees. *Proceedings of the National Academy of Sciences of the United States of America, 116*(14), 7101-7106. doi:10.1073/pnas.1818512116

Armstrong, E. (1980). A quantitative comparison of the hominoid thalamus: limbic nuclei anterior principalis and lateralis dorsalis. *American Journal of Physical Anthropology, 52*, 43-54.

Armstrong, E., Clarke, M. R., & Hill, E. M. (1987). Relative size of the anterior thalamic nuclei differentiates anthropoids by social system. *Brain, Behavior and Evolution, 30*, 263-271.

Barger, N., Hanson, K. L., Teffer, K., Schenker-Ahmed, N., & Semendeferi, K. (2014). Evidence for evolutionary specialization in human limbic structures. *Frontiers in Human Neuroscience, 8*. doi:10.3389/fnhum.2014.00277

Barger, N., Stefanacci, L., Schumann, C. M., Sherwood, C., Annese, J., Allman, J. M., Buckwalter, J. A., Hof, P. R., & Semendeferi, K. (2012). Neuronal Populations in the Basolateral Nuclei of the Amygdala Are Differentially Increased in Humans Compared With Apes: A stereological Study. *The Journal of Camparative Neurology, 520*, 3035-3054. doi:10.1002/cne.23118

Barger, N., Stefanacci, L., & Semendeferi, K. (2007). A comparative volumetric analysis of the amygdaloid complex and basolateral division in the human and ape brain. *American Journal of Physical Anthropology, 134*, 392-403. doi:10.1002/ajpa.20684

Bauernfeind, A. L., de Sousa, A. A., Avasthi, T., Dobson, S. D., Raghanti, M. A., Lewandowski, A. H., Zilles, K., Semendeferi, K., Allman, J. M., Craig, A. D., Hof, P. R., & Sherwood, C. C. (2013). A volumetric comparison of the insular cortex and its subregions in primates. *Journal of Human Evolution, 64*(4), 263-279. doi:10.1016/j.jhevol.2012.12.003

Bianchi, S., Stimpson, C. D., Bauernfeind, A. L., Schapiro, S. J., Baze, W. B., McArthur, M. J., Bronson, E., Hopkins, W. D., Semendeferi, K., Jacobs, B., Hof, P. R., & Sherwood, C. C. (2013). Dendritic Morphology of Pyramidal Neurons in the Chimpanzee Neocortex: Regional Specializations and Comparison to Humans. *Cerebral Cortex, 23*(10), 2429-2436. doi:10.1093/cercor/bhs239

Bianchi, S., Stimpson, C. D., Duka, T., Larsen, M. D., Janssen, W. G. M., Collins, Z., Bauernfeind, A. L., Schapiro, S. J., Baze, W. B., McArthur, M. J., Hopkins, W. D., Wildman, D. E., Lipovich, L., Kuzawa, C. W., Jacobs, B., Hof, P. R., & Sherwood, C. C. (2013). Synaptogenesis and development of pyramidal neuron dendritic morphology in the chimpanzee neocortex resembles humans. *Proceedings of the National Academy of Sciences of the United States of America, 110*, 10395-10401. doi:10.1073/pnas.1301224110

Buxhoeveden, D. P., Lefkowitz, W., Loats, P., & Armstrong, E. (1996). The linear organization of cell columns in human and nonhuman anthropoid Tpt cortex. *Anatomy and Embryology, 194*, 23-36.

Buxhoeveden, D. P., Switala, A. E., Roy, E., Litaker, M., & Casanova, M. F. (2001). Morphological differences between minicolumns in human and nonhuman primate cortex. *American Journal of Physical Anthropology, 115*(4), 361-371. doi:10.1002/ajpa.1092

Chen, H. B., Zhang, T., Guo, L., Li, K. M., Yu, X., Li, L. C., Hu, X. T., Han, J. W., Hu, X. P., & Liu, T. M. (2013). Coevolution of Gyral Folding and Structural Connection Patterns in Primate Brains. *Cerebral Cortex, 23*(5), 1208-1217. doi:10.1093/cercor/bhs113

Darwin, C. (2009). *On the Origin of Species*. New York, NY: Penguin Classics.

Donahue, C. J., Glasser, M. F., Preuss, T. M., Rilling, J. K., & Van Essen, D. C. (2018). Quantitative assessment of prefrontal cortex in humans relative to nonhuman primates. *Proceedings of the National Academy of Sciences of the United States of America, 115*(22), E5183-E5192. doi:10.1073/pnas.1721653115

Falk, D. (1980). Language, Handedness, and Primate Brains: Did the Australopithecines Sign? *American Anthropologist, 82*, 78-78.

Finlay, B. L., & Darlington, R. B. (1995). Linked regularities in the development and evolution of mammalian brains. *Science, 268*, 1578-1584.

Finlay, B. L., Darlington, R. B., & Nicastro, N. (2001). Developmental structure in brain evolution. *Behavioral and Brain Sciences, 24*, 263-308. doi:10.1017/S0140525X01373958

Gould, S. J., & Lewontin, R. C. (1979). The spandrels of San Marco and the Panglossian paradigm: a critique of the adaptationist program. *Proceedings of the Royal Society of London, 205*, 581-598.

Harvey, P. H., & Pagel, M. D. (1991). The comparative method for studying adaptation. In *The Comparative Method in Evolutionary Biology* (pp. 1-34). Oxford, UK: Oxford University Press.

Hecht, E. E., Gutman, D. A., Bradley, B. A., Preuss, T. M., & Stout, D. (2015). Virtual dissection and comparative connectivity of the superior longitudinal fasciculus in chimpanzees and humans. *Neuroimage, 108*, 124-137. doi:10.1016/j.neuroimage.2014.12.039

Hecht, E. E., Gutman, D. A., Preuss, T. M., Sanchez, M. M., Parr, L. A., & Rilling, J. K. (2013). Process Versus Product in Social Learning: Comparative Diffusion Tensor Imaging of Neural Systems for Action Execution-Observation Matching in Macaques, Chimpanzees, and Humans. *Cerebral Cortex, 23*(5), 1014-1024. doi:10.1093/cercor/bhs097

Hecht, E. E., Mahovetz, L. M., Preuss, T. M., & Hopkins, W. D. (2017). A neuroanatomical predictor of mirror self-recognition in chimpanzees. *Social Cognitive and Affective Neuroscience, 12*(1), 37-48. doi:10.1093/scan/nsw159

Hewes, G. W., Andrew, R. J., Carini, L., Choe, H., Gardner, R. A., Kortlandt, A., Krantz, G. S., McBride, G., Nottebohm, F., Pfeiffer, J., Rumbaugh, D. G., Steklis, H. D., Raliegh, M. J., Stopa, R., Suzuki, A., Washburn, S. L., & Wescott, R. W. (1973). Primate communication and the gestural origin of language *Current Anthropology, 14*, 5-24.

Hof, P. R., Nimchinsky, E. A., Perl, D. P., & Erwin, J. M. (2001). An unusual population of pyramidal neurons in the anterior cingulate cortex of hominids contains the calcium-binding protein calretinin. *Neuroscience Letters, 307*, 139-142.

Hopkins, W. D., & Avants, B. B. (2013). Regional and Hemispheric Variation in Cortical Thickness in Chimpanzees (Pan troglodytes). *Journal of Neuroscience, 33*(12), 5241-5248. doi:10.1523/jneurosci.2996-12.2013

Hopkins, W. D., Li, X., Crow, T., & Roberts, N. (2017). Vertex- and atlas-based comparisons in measures of cortical thickness, gyrification and white matter volume between humans and chimpanzees. *Brain Structure & Function, 222*(1), 229-245. doi:10.1007/s00429-016-1213-1

Hopkins, W. D., Li, X., & Roberts, N. (2019). More intelligent chimpanzees (Pan troglodytes) have larger brains and increased cortical thickness. *Intelligence, 74*, 18-24. doi:10.1016/j.intell.2018.11.002

Hopkins, W. D., Lyn, H., & Cantalupo, C. (2009). Volumetric and Lateralized Differences in Selected Brain Regions of Chimpanzees (Pan troglodytes) and Bonobos (Pan paniscus). *American Journal of Primatology, 71*(12), 988-997. doi:10.1002/ajp.20741

Issa, H. A., Staes, N., Diggs-Galligan, S., Stimpson, C. D., Gendron-Fitzpatrick, A., Taglialatela, J. P., Hof, P. R., Hopkins, W. D., & Sherwood, C. C. (2019). Comparison of bonobo and

chimpanzee brain microstructure reveals differences in socio-emotional circuits. *Brain Structure & Function, 224*(1), 239-251. doi:10.1007/s00429-018-1751-9

Lew, C. H., Hanson, K. L., Groeniger, K. M., Greiner, D., Cuevas, D., Hrvoj-Mihic, B., Schumann, C. M., & Semendeferi, K. (2019). Serotonergic innervation of the human amygdala and evolutionary implications. *American Journal of Physical Anthropology, 170*(3), 351-360. doi:10.1002/ajpa.23896

Li, X., Chen, H. B., Zhang, T., Yu, X., Jiang, X., Li, K. M., Li, L. C., Razavi, M. J., Wang, X. Q., Hu, X. T., Han, J. W., Guo, L., Hu, X. P., & Liu, T. M. (2017). Commonly preserved and species-specific gyral folding patterns across primate brains. *Brain Structure & Function, 222*(5), 2127-2141. doi:10.1007/s00429-016-1329-3

Maynard Smith, J., Burian, R., Kauffman, S., Albrech, P., Campbell, J., Goodwin, B., Lande, R., Raup, D., & Wolpert, L. (1985). Developmental constraints on evolution: a perspective from the mountain lake *The Quarterly Review of Biology 60*(3), 265-287.

Miller, D. J., Duka, T., Stimpson, C. D., Schapiro, S. J., Baze, W. B., McArthur, M. J., Fobbs, A. J., Sousa, A. M. M., Sestan, N., Wildman, D. E., Lipovich, L., Kuzawa, C. W., Hof, P. R., & Sherwood, C. C. (2012). Prolonged myelination in human neocortical evolution. *Proceedings of the National Academy of Sciences of the United States of America, 109*(41), 16480-16485. doi:10.1073/pnas.1117943109

Palomero-Gallagher, N., & Zilles, K. (2019). Differences in cytoarchitecture of Broca's region between human, ape and macaque brains. *Cortex, 118*, 132-153. doi:10.1016/j.cortex.2018.09.008

Parker, S. T., & R., G. K. (1979). A developmental model for the evolution of language and inteligence in early hominids. *The Behavioral and Brain Sciences, 2*, 367-406.

Pope, S. M., Taglialatela, J. P., Skiba, S. A., & Hopkins, W. D. (2018). Changes in Frontoparietotemporal Connectivity following Do-As-I-Do Imitation Training in Chimpanzees (Pan troglodytes). *Journal of Cognitive Neuroscience, 30*(3), 421-431. doi:10.1162/jocn_a_01217

Preuss, T. M. (2009). Primate brain evolution. In J. H. Kass, G. F. Striedter, J. L. Rubenstien, T. H. Bullock, L. Krubitzer, & T. Preuss (Eds.), *Evolutionary Neuroscience* (pp. 794-825). Oxford, UK: Academic Press.

Raghanti, M. A., Edler, M. K., Stephenson, A. R., Wilson, L. J., Hopkins, W. D., Ely, J. J., Erwin, J. M., Jacobs, B., Hof, P. R., & Sherwood, C. C. (2016). Human-Specific Increase of Dopaminergic Innervation in a Striatal Region Associated With Speech and Language: A Comparative Analysis of the Primate Basal Ganglia. *Journal of Comparative Neurology, 524*(10), 2117-2129. doi:10.1002/cne.23937

Raghanti, M. A., Simic, G., Watson, S., Stimpson, C. D., Hof, P. R., & Sherwood, C. C. (2011). COMPARATIVE ANALYSIS OF THE NUCLEUS BASALIS OF MEYNERT AMONG PRIMATES. *Neuroscience, 184*, 1-15. doi:10.1016/j.neuroscience.2011.04.008

Raghanti, M. A., Spocter, M. A., Stimpson, C. D., Erwin, J. M., Bonar, C. J., Allman, J. M., Hof, P. R., & Sherwood, C. C. (2009). SPECIES-SPECIFIC DISTRIBUTIONS OF TYROSINE HYDROXYLASE-IMMUNOREACTIVE NEURONS IN THE PREFRONTAL CORTEX OF ANTHROPOID PRIMATES. *Neuroscience, 158*(4), 1551-1559. doi:10.1016/j.neuroscience.2008.10.058

Raghanti, M. A., Stimpson, C. D., Marcinkiewicz, J. L., Erwin, J. M., Hof, P. R., & Sherwood, C. C. (2008a). Cholinergic innervation of the frontal cortex: Differences among humans, chimpanzees, and macaque monkeys. *Journal of Comparative Neurology, 506*(3), 409-424. doi:10.1002/cne.21546

Raghanti, M. A., Stimpson, C. D., Marcinkiewicz, J. L., Erwin, J. M., Hof, P. R., & Sherwood, C. C. (2008b). Cortical dopaminergic innervation among humans, chimpanzees, and macaque monkeys: A comparative study. *Neuroscience, 155*(1), 203-220. doi:10.1016/j.neuroscience.2008.05.008

Raghanti, M. A., Stimpson, C. D., Marcinkiewicz, J. L., Erwin, J. M., Hof, P. R., & Sherwood, C. C. (2008c). Differences in cortical dopaminergic innervation among humans, chimpanzees, and Macaque monkeys: A comparative study. *American Journal of Physical Anthropology*, 176-176.

Raghanti, M. A., Stimpson, C. D., Marcinkiewicz, J. L., Erwin, J. M., Hof, P. R., & Sherwood, C. C. (2008d). Differences in cortical serotonergic innervation among humans, chimpanzees, and macaque monkeys: A comparative study. *Cerebral Cortex, 18*(3), 584-597. doi:10.1093/cercor/bhm089

Rilling, J. K., Glasser, M. F., Preuss, T. M., Ma, X., Zhao, T., Hu, X., & Behrens, T. E. (2007). The evolution of the arcuate fasciculus revealed with comparative DTI. *Nature Neuroscience, 11*, 426-428.

Rilling, J. K., Scholz, J., Preuss, T. M., Glasser, M. F., Errangi, B. K., & Behrens, T. E. (2012). Differences between chimpanzees and bonobos in neural systems supporting social cognition. *Social Cognitive and Affective Neuroscience, 7*(4), 369-379. doi:10.1093/scan/nsr017

Rilling, J. K., & Seligman, R. A. (2002). A quantitative morphometric comparative analysis of the primate temporal lobe. *Journal of Human Evolution, 42*(5), 505-533. doi:10.1006/jhev.2001.0537

Rogers, C. N., Ross, A. P., Sahu, S. P., Siegel, E. R., Dooyema, J. M., Cree, M. A., Stopa, E. G., Young, L. J., Rilling, J. K., Albers, H. E., & Preuss, T. M. (2018). Oxytocin- and arginine

vasopressin-containing fibers in the cortex of humans, chimpanzees, and macaques. *American Journal of Primatology, 80*, e22875. doi:10.1002/ajp.22875

Sakai, T., Matsui, M., Mikami, A., Malkova, L., Hamada, Y., Tomonaga, M., Suzuki, J., Tanaka, M., Miyabe-Nishiwaki, T., Makishima, H., Nakatsukasa, M., & Matsuzawa, T. (2013). Developmental patterns of chimpanzee cerebral tissues provide important clues for understanding the remarkable enlargement of the human brain. *Proceedings of the Royal Society B-Biological Sciences, 280*(1753). doi:10.1098/rspb.2012.2398

Sakai, T., Mikami, A., Tomonaga, M., Matsui, M., Suzuki, J., Hamada, Y., Tanaka, M., Miyabe-Nishiwaki, T., Makishima, H., Nakatsukasa, M., & Matsuzawa, T. (2011). Differential Prefrontal White Matter Development in Chimpanzees and Humans. *Current Biology, 21*(16), 1397-1402. doi:10.1016/j.cub.2011.07.019

Schenker, N. M., Buxhoeveden, D. P., Blackmon, W. L., Amunts, K., Zilles, K., & Semendeferi, K. (2008). A comparative quantitative analysis of cytoarchitecture and minicolumnar organization in Broca's area in humans and great apes. *Journal of Comparative Neurology, 510*(1), 117-128. doi:10.1002/cne.21792

Schenker, N. M., Desgouttes, A. M., & Semendeferi, K. (2005). Neural connectivity and cortical substrates of cognition in hominoids. *Journal of Human Evolution, 49*(5), 547-569. doi:10.1016/j.jhevol.2005.06.004

Schenker, N. M., Hopkins, W. D., Spocter, M. A., Garrison, A. R., Stimpson, C. D., Erwin, J. M., Hof, P. R., & Sherwood, C. C. (2010). Broca's Area Homologue in Chimpanzees (Pan troglodytes): Probabilistic Mapping, Asymmetry, and Comparison to Humans. *Cerebral Cortex, 20*(3), 730-742. doi:10.1093/cercor/bhp138

Semendeferi, K., Armstrong, E., Schleicher, A., Zilles, K., & Van Hoesen, G. W. (1998). Limbic frontal cortex in hominoids: A comparative study of area 13. *American Journal of Physical Anthropology, 106*(2), 129-155. doi:10.1002/(sici)1096-8644(199806)106:2<129::Aid-ajpa3>3.3.Co;2-5

Semendeferi, K., Armstrong, E., Schleicher, A., Zilles, K., & Van Hoesen, G. W. (2001). Prefrontal cortex in humans and apes: A comparative study of area 10. *American Journal of Physical Anthropology, 114*(3), 224-241. doi:10.1002/1096-8644(200103)114:3<224::Aid-ajpa1022>3.0.Co;2-i

Semendeferi, K., Barger, N., & Schenker, N. (2010). Brain reorganization in humans and apes. In D. Broadfield, K. Yuan, K. Schick, & N. Toth (Eds.), *The Human Brain Evolving: Paleoneurological Studies in Honor of Ralph L. Holloway* (pp. 119-149). Gosport, IN: Stone Age Institute Press.

Semendeferi, K., & Damasio, H. (2000). The brain and its main anatomical subdivisions in living hominoids using magnetic resonance imaging. *Journal of Human Evolution, 38*(2), 317-332. doi:10.1006/jhev.1999.0381

Semendeferi, K., Damasio, H., Frank, R., & Van Hoesen, G. W. (1997). The evolution of the frontal lobes: a volumetric analyses based on three-dimensional reconstructions of magnetic resonance scans of human and ape brains. *Journal of Human Evolution, 32*(4), 375-388. doi:10.1006/jhev.1996.0099

Semendeferi, K., Teffer, K., Buxhoeveden, D. P., Park, M. S., Bludau, S., Amunts, K., Travis, K., & Buckwalter, J. (2011). Spatial Organization of Neurons in the Frontal Pole Sets Humans Apart from Great Apes. *Cerebral Cortex, 21*(7), 1485-1497. doi:10.1093/cercor/bhq191

Smaers, J. B., Schleicher, A., Zilles, K., & Vinicius, L. (2010). Frontal White Matter Volume Is Associated with Brain Enlargement and Higher Structural Connectivity in Anthropoid Primates. *Plos One, 5*(2). doi:10.1371/journal.pone.0009123

Smaers, J. B., Steele, J., Case, C. R., Cowper, A., Amunts, K., & Zilles, K. (2011). Primate Prefrontal Cortex Evolution: Human Brains Are the Extreme of a Lateralized Ape Trend. *Brain Behavior and Evolution, 77*(2), 67-78. doi:10.1159/000323671

Spocter, M. A., Hopkins, W. D., Barks, S. K., Bianchi, S., Hehmeyer, A. E., Anderson, S. M., Stimpson, C. D., Fobbs, A. J., Hof, P. R., & Sherwood, C. C. (2012). Neuropil distribution in the cerebral cortex differs between humans and chimpanzees. *Journal of Comparative Neurology, 520*(13), 2917-2929. doi:10.1002/cne.23074

Spocter, M. A., Hopkins, W. D., Garrison, A. R., Bauernfeind, A. L., Stimpson, C. D., Hof, P. R., & Sherwood, C. C. (2010). Wernicke's area homologue in chimpanzees (Pan troglodytes) and its relation to the appearance of modern human language. *Proceedings of the Royal Society B-Biological Sciences, 277*(1691), 2165-2174. doi:10.1098/rspb.2010.0011

Stephenson, A. R., Edler, M. K., Erwin, J. M., Jacobs, B., Hopkins, W. D., Hof, P. R., Sherwood, C. C., & Raghanti, M. A. (2017). Cholinergic Innervation of the Basal Ganglia in Humans and Other Anthropoid Primates. *Journal of Comparative Neurology, 525*(2), 319-332. doi:10.1002/cne.24067

Stimpson, C. D., Barger, N., Taglialatela, J. P., Gendron-Fitzpatrick, A., Hof, P. R., Hopkins, W. D., & Sherwood, C. C. (2016). Differential serotonergic innervation of the amygdala in bonobos and chimpanzees. *Social Cognitive and Affective Neuroscience, 11*(3), 413-422. doi:10.1093/scan/nsv128

Striedter, G. F. (2005). *Principles of Brain Evolution*. Sunderland, MA: Sinauer Associates Incorporated.

Striedter, G. F. (2009). History of ideas on brain evolution. In J. H. Kass, G. F. Striedter, J. L. Rubenstien, T. H. Bullock, L. Krubitzer, & T. Preuss (Eds.), *Evolutionary Neuroscience* (pp. 3-17). Oxford, UK: Academic Press.

Teffer, K., Buxhoeveden, D. P., Stimpson, C. D., Fobbs, A. J., Schapiro, S. J., Baze, W. B., McArthur, M. J., Hopkins, W. D., Hof, P. R., Sherwood, C. C., & Semendeferi, K. (2013). Developmental Changes in the Spatial Organization of Neurons in the Neocortex of Humans and Common Chimpanzees. *Journal of Comparative Neurology*, *521*(18), 4249-4259. doi:10.1002/cne.23412

Van Essen, D. C. (1997). A tension-based theory of morphologenesis and compact wiring in the central nervous system. *Nature, 385*, 313-318.

Zilles, K., Armstrong, E., Moser, K. H., Schleicher, A., & Stephan, H. (1989). Gyrification in the Cerbral Cortex of Primates. *Brain, Behavior and Evolution, 34*, 143-150.

Zilles, K., Schleicher, A., & Kretschmann, H. (1978). Automatic morphometric analysis of retrograde changes in the n. facialis at different ontogenetic stages in the rat. *Cell and Tissue Research 190*, 285-299.