Body Asymmetries: Incidence, Etiology and Clinical Implications

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Abstract: Symmetry is defined as correspondence in size, shape and relative position of parts on opposite sides of a dividing line or median plane. Although the human body has a symmetrical appearance when viewed externally, most internal organs are asymmetrical with respect to the left and right sides. Human body shows anatomical as well as functional asymmetries: some of these are of great clinical significance. This paper aims to integrate the general knowledge of incidence, etiologic factors, and clinical implications of body asymmetries. Knowledge and understanding of these asymmetries is important to achieve a good diagnosis and focus on an appropriate treatment and management plan.

Key words: Fluctuating asymmetry, directional asymmetry, functional asymmetry, skeletal asymmetry, vascular asymmetry.

INTRODUCTION

The word symmetry is derived from the Greek word symmetria which means ‘of like measure’. Symmetry is defined as correspondence in size, shape and relative position of parts on opposite sides of a dividing line or median plane. Asymmetry is described as a lack or absence of symmetry.

Does a median sagittal plane divide the human body into two equal halves? The answer is ‘no’. Although the human body has a symmetrical appearance when viewed externally, as a result of exact measurements taken from a great number of cadavers and living subjects, it has been established that the two halves of the human body are in reality never symmetrical, e.g. the right lung is shorter and wider than the left lung and is trilobed, while the left lung is bilobed. The heart is more leftward with the apex pointing downwards and to the left. The liver and gallbladder are located on the right and spleen lies on the left in the abdominal cavity. The right kidney is positioned lower than the left kidney. The right suprarenal gland is pyramidal shaped and the left is crescent shaped. The right subclavian artery arises from the brachiocephalic trunk and the left arises from the arch of aorta. The right recurrent laryngeal nerve arises from vagus in the neck, while the left arises in the thorax. The left colic flexure lies at a higher level than the right. The left gonadal vein and the left suprarenal vein drain into the left renal vein, while on the right side, both of these veins drain into the inferior vena cava. The superior sagittal venous sinus continues as the right and the straight sinus continues as the left transverse venous sinus. Even the left and right hemispheres of the brain have subtle but important physical differences.

Humans show bilateral symmetry in paired morphological traits such as ear size, digit length and breast volume. Perfect symmetry may be disturbed by a number of intrinsic and extrinsic factors, including the secretion of hormones such as oestrogen (Manning et al. 1996). The biologic principle of bilateral symmetry is never manifested with mathematical precision, and even in fully homologous organs in the two halves of the body there are almost invariably small differences. The small, random deviations from perfect symmetry that result from such factors are termed fluctuating asymmetry (FA). FA is defined as deviation from perfect symmetry in bilateral physical traits that do not display any directional tendency, and that are close to being normally distributed (Valen, 1962). FA in such traits as ear size and digit length is related to health measures including body mass index (BMI) in young women and men (Milne et al. 2003) Fluctuating asymmetry is a type of developmental instability; it is a measure of how much an individual varies from the typical pattern of bilateral symmetry (Møller, 1999). Fluctuations are thought to represent inability to tolerate stressors, either genetic or environmental (Møller & Pomiankowski, 1993). Population-level deviations from bilateral symmetry that are unimodal and significantly different from symmetry are called directional asymmetries. Examples are the conspicuous asymmetry of internal organs and the more subtle asymmetry of the human brain (Toga & Thompson, 2003). This is especially found in structures related to the upper limb as a consequence of its freedom from locomotor constraints (Trinkaus et al., 1994).

The aim of this review was to study the incidence, possible etiological factors and the clinical significance, (e.g. prediction of occurrence, diagnosis, course, management, prognosis and prevention of certain diseases), of asymmetries in structures that are bilaterally symmetrical otherwise.
**Brain Asymmetries:**

In humans, the two brain hemispheres differ structurally, functionally, and behaviorally. Asymmetries in the brain’s functional layout, cytoarchitecture, and neurochemistry have also been correlated with gender, age, a variety of genetic factors, hormonal influences and asymmetrical behavioral traits, such as handedness, auditory perception, motor preferences, and sensory acuity. The gross anatomy and functional layout of the brain are organized asymmetrically, with hemispheric specializations for key aspects of language and motor function. These asymmetries are first observed around 29-31 weeks gestational age (Toga & Thompson, 2003). Differing developmental programmes structure the two hemispheres well into childhood and beyond, leading to lateralized differences in maturational rates, dendritic arborization, metabolism, and functional activation (Toga & Thompson, 2003). In humans, inbreeding (Markow & Martin, 1993), poor health conditions, and various neurological disorders, such as schizophrenia, attention deficit disorder, developmental delays in childhood and Down syndrome are positively associated with fluctuating asymmetries (Mellor, 1992; Burton et al., 2002, 2003; Naugler & Ludman, 1996; Barden, 1980). Significant difference in the degree of asymmetry was found between males and females (Kulynych et al., 1994; Witelson, 1991; Witelson & Kigar, 1992). The degree of asymmetry was either larger or less variable in males than in females and it was also reported that the said asymmetries in right-handed subjects were either larger or less variable than in left-handed one (Amunts et al., 2000; Bear et al., 1986; Watkins et al., 2001). Asymmetric areas have been reported to have less interhemispheric connections (Galaburda et al., 1990). Specialization of language at the left hemisphere being the best-known functional asymmetry, it can be speculated that some morphological asymmetries could be related to other functional hemispheric specialization (Rakic, 1988, 2001). Anatomical asymmetries may help to explain the range of human talents, recovery from acquired disorders of language function, certain childhood learning disabilities, and some dementing illnesses of middle life (Galaburda et al., 1978).

**Sulcal & Gyral Pattern:**

Sulci and gyri provide a natural topographic partition of the cortical anatomy. Additionally, the junctional zones between adjacent functional or architectonic fields frequently run along the bed of major or minor cortical sulci (Rademacher et al., 1993; Roland & Zilles, 1994; Sanides, 1962; Watson et al., 1993). Tremendous variability in the size, shape and configuration of cortical gyri and sulci have been well demonstrated (Damasio & Damasio, 1989; Evans et al., 1992; Keyserlingk et al., 1988; Mazziotto et al., 1995; Steinmetz et al., 1990a; Steinmetz et al., 1990b; Steinmetz et al.1990c; Talairach et al., 1967; Talairach and Tournoux, 1988; Thompson et al., 1996; Zilles et al., 1997). The pattern of sulcal and gyral folds exhibits structural complexity and large intersubject variability (Im et al., 2010). Asymmetries of the planum temporale and sulci in the temporal region have been reported in the human brain as early as 29 weeks of gestation (Chi et al., 1977a, b). The superior temporal sulcus (STS) is the main sulcal landmark of the external temporal cortex and is very important for functional (posterior language areas on the left) mapping and surgery. Ochiai et al. (2004) found that the 3D architecture of the STs was significantly different between right and left hemispheres. Im et al. (2010) noted significant asymmetry in the frequency and spatial variance of sulcal pits in the superior temporal sulcus of the two hemispheres. The frequency of sulcal pits was significantly greater in the left than in the right hemisphere.

Another well-established hemispheric asymmetry includes the trajectory of the Sylvian fissure which, at its posterior limit, curves upwards more anteriorly on the right than on the left hemisphere (Geschwind & Levitsky, 1968). Interhemispheric differences were found in the length and angulation of the sylvian fissure, with the left being longer and running more horizontal than the right (Cunningham, 1892; Eberstaller, 1890; Talairach et al., 1967; Szikla et al., 1977; Steinmetz et al., 1989a; Steinmetz et al., 1989 b). Asymmetries in the auditory regions and in the sylvian fissures are present even in the fetus. LeMay & Culebras (1972) showed that the end of the sylvian fissure was already higher on the right than on the left in fetal brains, indicating that asymmetry of the sylvian fissure already exists at early stages of ontogeny. Steinmetz et al. (1990a,b,c) showed that additionally the left parietal operculum was larger, and that the local sulcal pattern was different depending on the side, and that these asymmetries were related to handedness (Steinmetz et al., 1991; White et al., 1994). Conversely, the parietale operculum has been shown to be larger in the right hemisphere (Gannon et al., 2005; Jäncke et al., 1994). The study of central sulcus depth revealed that, in right-handers, the left central sulcus was deeper than the right one (and vice versa in lefthanders) and that the neuropil volume of the left Brodmann’s area 4 was thicker in the right-hand suggested suggesting an association of hand preference with increased connectivity and increased intrasulcal surface of the pre-central gyrus in the dominant hemisphere (Amunts et al., 1996).

Cykowski et al. (2008) used an automated, approach to study the sulcal depth of the central sulcus (CS) and demonstrated that the superior CS in men and the midpoint of the CS in women had leftward asymmetry. Other MR morphometry studies used manual segmentation to explore CS depth asymmetry (Amunts et al., 2000; Amunts et al., 1996; Davatzikos & Bryan, 2002), and reported handedness effects that showed the dominant hemisphere to be deeper than the non-dominant. Boni et al. (2007) reported that in men the left lateral...
The paracingulate sulcus was found more frequently in the left than in the right hemisphere (Paus et al., 1996). The paracingulate sulcus was found more frequently in the left than in the right hemisphere (Paus et al., 1996). The paracingulate sulcus was found more frequently in the left than in the right hemisphere (Paus et al., 1996).

The cortical areas underlying auditory function show the most evident anatomical asymmetries between the left and right hemisphere such as the Heschl’s gyrus and the planum temporale (Dorsaint-Pierre et al., 2006; Kolb & Whishaw, 2003). However, neuroanatomical, neurophysiological, and neuropsychological evidence suggest that, although there is an auditory representation of both ears in both cortices, the contralateral representations exceed the ipsilateral ones (King & Carlisle, 1995; Popper & Fay, 1992). The volume of the Heschl gyrus with the primary auditory cortex was found to be larger in the left than in the right hemisphere (Penhune et al., 1996; Rademacher et al., 1993), which was interpreted to result from larger amounts of white matter underlying the gyrus (Galaburda & Geschwind, 1981; Penhune et al., 1996). Furthermore, the degree of HG asymmetry across individuals predicts to some extent both functional activation patterns (Warrier et al., 2009) and behavioral ability to learn novel speech sounds (Golestani & Zatorre, 2004; Wong, et al., 2008). An in vivo MRI morphometry study reported more white substance in the left primary auditory cortex as compared to the right side, whereas the gray matter did not differ significantly (Penhune et al., 1996). The distance between cell columns of multiple areas of the auditory cortex, with exception of primary auditory cortex, was remarkably larger in the left than in the right hemispheres, as demonstrated in Golgi-impregnated sections, suggesting more space for neuropil in the left than in the right hemisphere (Seldon, 1981a, b). Left-right asymmetries of the transverse temporal (Heschl) gyri and the temporal plane become recognizable by 31 weeks’ gestation (Chi et al., 1977a).

A second area of left dominance is the temporal planum, a region in the posterior portion of the superior temporal sulcus and in particular the supramarginal gyrus (LeMay, 1976; Bradshaw, 1988), included in Wernicke’s area and related to speech integration. The planum largely corresponds to cytoarchitectonic area 42 (Brodmann, 1909) or TB (von Economo & Koskinas, 1925). Pfeifer (1911) and von Economo & Horn (1930) were among the first to observe that the left planum temporale was often larger than the right. Later several studies (postmortem and in vivo) revealed a pronounced leftward asymmetry with respect to the length, the area, and the volume of the planum (Geschwind & Levitsky, 1968; Wada et al., 1975; Chi et al. 1977b; Pfeiffer et al., 1993; Steinmetz et al., 1990; Shapleske et al., 1999; Steinmetz, 1996). A reduced leftward (but not inverted) asymmetry of the planum temporale was found in healthy left-handers as compared to right-handers (Jäncke & Steinmetz, 2004; Steinmetz, 1996). Geschwind & Levitsky (1968) suggested that this feature was related to language laterality.

Left and right plana also differed with respect to choline acetyltransferase activity, which was higher in the left than in the right hemisphere as shown in a sample of four human brains (Amaducci et al., 1981). Interhemispheric asymmetries, with the left planum being larger than the right, were recognizable by 31 weeks of gestation, as shown in a postmortem study with a sample of 207 fetal brains (Chi et al., 1977). Furthermore, asymmetries have been documented in young brains, with 56-79% of the fetuses or infants measured having a larger left planum (Witelson & Pallie, 1973; Wada et al., 1975; Chi et al., 1977). Asymmetries in Broca’s area (areas 44 and 45 of Brodmann) have also been reported. Areas 44 and 45 are key regions of the anterior language region, Broca’s region. They occupy the pars opercularis and pars triangularis, respectively. Broca’s area was found to be larger in the left hemisphere (Amunts et al., 1999; Annett, 1970; Falzi, Perrone, & Vignolo, 1982; Foundas et al., 1996; Geschwind & Galaburda, 1985a). The volumes of left area 44 were greater than those of the right hemisphere as shown in two postmortem studies (Amunts et al., 1999; Galaburda, 1980). The volumes of area 45 did not differ significantly between the hemispheres (Amunts et al., 1999), although for six of the ten subjects (including all females), the volume of area 45 was greater in the left hemisphere than the right (Amunts et al., 1999; Uylings et al., 2006). The large volume is mainly related to the increase of the cortex buried in sulci (Falzi et al., 1982). Significant interhemispheric differences in cytoarchitecture are already present in 1-year-old infants (Amunts et al., 2003). Posterior fusiform, angular gyri and the anterior part of the insula have also been described as larger on the left (Eidelberg & Galaburda, 1984; McDonald et al., 2000; Niznikiewicz et al., 2000).

In modern and fossil humans the most common and distinctive general pattern is a dominance of the right frontal and left occipital lobes namely right frontal (RF) and left occipital (LO) petalias (LeMay, 1976; Holloway & De La Coste- Lareymonde,1982). These asymmetries initially noticed on the inner aspect of the skull (LeMay, 1977, 1984 Chiu & Damasio, 1980; Gundara & Zivanovic, 1968; LeMay, 1976) have been confirmed by much more sophisticated MR analysis (Falk, et al 1991). In humans, the right frontal pole protrudes farther (Hadziselimovic & Cus, 1966). Lyttelton, et al. (2009) confirmed hemispheric asymmetries in frontal and occipital petalialsa and also revealed striking leftward increase in surface area of the supramarginal gyrus (peak effect 18%), compared with a smaller increase in the left Heschl's gyrus and planum temporale region and a rightward increase in surface area (peak effect 10%) in a band around the medial junction between the occipital lobe, and parietal and temporal lobes. This pattern is characteristic for male right-handers (Kertesz et al., 1990; LeMay & Kido, 1978). Left-handers generally show a smaller degree of asymmetry and frequently
can resent a left frontal-right occipital petalial (LeMay, 1977). A similar left dominance for right-handers and smaller asymmetry for left-handers has also been recorded in the precentral gyrus (Foundas et al., 1998).

Interhemispheric differences of prefrontal cortex have been reported by Whittet al. (2008). Analyses of the neuronal density, size, and shape in Brodmann’s areas 9 and 10 revealed a larger density of neurons in the left as compared to the right hemisphere; pyramidal neurons of layer III were larger on the left and more spherical than the right side (Cullen et al., 2006).

Asymmetry has been reported with respect to the hippocampus, the cingulate gyrus, the amygdala, and the habenula. The cingulate cortex shows ED signs of interhemispheric asymmetry. The volume of the right anterior cingulated cortex has been shown to be larger than the left (Pujol et al., 2002), and there is evidence of significant sulcal pattern asymmetries in this region (Paus et al., 1996). Hutsler et al., (1998) manually segmented the cingulate and post-central gyrus in mesh representations of the left and right hemispheres of ten right-handed subjects. Although the results did not reach statistical significance, the size of the cingulate gyrus showed a right greater than left tendency and the post-central gyrus showed a left greater than right tendency. A significant leftward asymmetry was reported in the thickness of the anterior segment and significant leftward asymmetry in the surface area of the posterior segment in normal and schizophrenic (Wang et al., 2007). Another study analyzed the surface area of an anterior and a posterior cingulate region; a rightward asymmetry was reported for the anterior cingulate region, which was more frequently found in females than in males. The posterior cingulate region did not differ between the hemispheres (Pujol et al., 2002).

It has been suggested that the amygdalae are both structurally (Szabo et al., 2001) and functionally asymmetrical (Baas et al., 2004). Most studies that have examined hippocampal and amygdala volumes in normal adult participants vary considerably with regard to the degree of volumetric asymmetry as well as the absolute intrahemispheric volumes reported (Bhatia et al., 1993; Bigler et al., 1997; Cendes et al., 1993; Convit et al., 1999; Kälviäinen et al., 1997a, b; Szesko et al., 1999; Watson et al., 1992; Whitworth et al., 1998). Hippocampal asymmetry has received more attention among researchers than amygdala asymmetry, with most studies reporting either a larger right hippocampus or no left-right hippocampal asymmetry. Brierley, Shaw, & David (2002) conducted a meta-analysis of MRI-based amygdala volumes and found no significant difference between left and right amygdala volumes in normal individuals. These in vivo results are in marked contrast to post-mortem examinations of amygdala volumes, which suggest that a right greater than left asymmetry exists in normal individuals (Gloor, 1997; Murphy et al., 1987). Pedraza et al. (2004), did a systematic analysis of hippocampal and amygdala volumetric asymmetry in normal adults using metaanalytic procedures, and revealed a significant volumetric asymmetry in amygdala and hippocampus, suggesting that the right amygdala & right hippocampus are reliably larger than the left amygdala & hippocampus in normal adults.

Interhemispheric asymmetry has been found in several components of the motor and sensory systems — for example, the caudate nucleus (Watkins et al., 2001), the cerebellum (Snyder et al., 1995), and the sensory and motor cortices. Tremols et al. (2008) compared the caudate heads and bodies of an attention deficit-hyperactivity disorder (ADHD) group with those of a control group and found a significantly larger left caudate head and a significantly bigger caudate right body and right head + body in control group. White et al. (1994) found that the regions of the cerebral cortex which control each upper limb do indeed differ in volume by about 7%. Thus, in right-handed people the left somatomotor cortex controlling the right upper limb is about 7% larger than the corresponding cortex of the right side of the brain (motor pathways to the limbs cross the midline). Asymmetric mammillary bodies have been reported in an average of 20% of healthy subjects (Kim et al., 1995; Ng et al. 1997). Deasy et al. (2002) showed ipsilateral asymmetrically small thalamus, fornix and mammillary body in patients with mesial temporal sclerosis. Boni et al. (2007) concluded, on the basis of the measurements made, that there are differences between the right and left temporal lobes. Their results demonstrated that the temporal plane was 0.9 cm larger on the left in 65% of the sample, larger on the right in 11% of the sample and equal in 24% of the sample.

White Matter:

White et al. (1997) reported that the pyramidal tract seemed to be symmetrical, while an earlier study found priority for pyramidal tract fibers coming from the left hemisphere (Yakovlev & Rakic, 1966). Nathan and colleagues reported asymmetry in the size of the lateral and anterior corticospinal tract (Nathan et al., 1990). They found that the right corticospinal tract was larger, which is consistent with the size left-larger than right difference in cortex. The anterior corticospinal tract was larger on the right side. It is largely uncrossed, which suggests that the originating cortex is larger on the right than on the left side. Flechsig (1876) found that in the majority of specimens (75%) most of the CST fibers cross from one side to the other, but the crossing pattern differs between the two sides in 40% of the brains. Among these asymmetrical cases, the uncrossed component was more often larger on the right side of the spinal cord than on the left. Voxel-based morphometry (VBM) studies of MRI structural images (e.g., T1 weighted) show larger white matter volumes in the left internal capsule without a clear association with handedness (Good et al., 2001; Hervé et al., 2006). Using techniques of quantitative cytoarchitectonic and myeloarchitectonic image analysis, the identifiable pre-central component of
the pyramidal tract revealed the larger volume of the descending cortical motor fibres in the left hemisphere in human post-mortem brains (Rademacher et al., 2001a,b).

The lateral corticospinal pathway from motor cortex to the spinal motoneurons controlling the fingers and hand provides the capacity for independent control of the digits, and skilled use of the hand for fine motor tasks (Porter & Lemon 1993). Approximately 90% of humans prefer to use the right hand for unimanual tasks (Hardyck & Petrinovich 1977). Lateral differences in anatomical (Amunts et al. 1996; Foundas et al., 1997) and physiological (MacDonell et al. 1991; Triggs et al., 1994; Triggs et al., 1999) properties of motor cortex or the corticospinal system have been described which are related to hand preference. Using magnetoencephalography (MEG), Volkmann et al., (1998) found a larger spatial distribution of primary motor cortical activity opposite the preferred hand of right- (RH) and lefthanded (LH) subjects during simple tasks with the fingers, and a relation between motor cortex asymmetry and relative hand skill. The authors interpreted the MEG findings to indicate that similar numbers of pyramidal neurons were active on each side, but dispersed over a larger area of motor cortex opposite the preferred (more skilled) hand (Volkmann et al. 1998).

Eidelberg & Galaburda (1982) showed a slight rightward asymmetry of the medial geniculate nucleus and a leftward asymmetry of the lateralis posterior nucleus, which projects to the inferior parietal lobule. Bürgel and colleagues (2006) showed asymmetries in the position and size of the human optic radiation using post-mortem dissections. In their sample of 10 subjects, nine showed a leftward asymmetry in the volume of the lateral geniculate and optic radiations. Interhemispheric differences in the inferior frontal cortex are supplemented by white matter asymmetries. The uncinate fascicle, a major fiber tract that is assumed to connect the inferior frontal cortex with anterior temporal cortex, was asymmetrical in brains of both males and females; it was 27% larger and contained 33% more fibers in the right than in the left hemisphere (Highley et al., 2002). VBM studies of the white matter region containing uncinate fibers (i.e., anterior floor of the external capsule) are contrasting with both leftward (Hervé et al., 2006) and rightward (Good et al., 2001) asymmetry reported.

The white matter regions containing fibers of the arcuate fasciculus are larger on the left compared to right (Good et al., 2001; Hervé et al., 2006). In vivo structural markers of hemispheric asymmetries in infants from 1 to 4 months of age, with diffusion tensor imaging demonstrated early leftward asymmetries in the arcuate fasciculus and in the cortico-spinal tract. These results suggest that the early macroscopic geometry, microscopic organization, and maturation of these white matter bundles are related to the development of later functional lateralization (Dubois et al. 2009).

Ventricular System:

Asymmetries of the lateral ventricles are present early in development and appear to be a normal brain variant (Achiron et al., 1997; Lodin, 1968). Several authors have reported that a significant proportion of normal children or neonates had asymmetric lateral ventricles on pneumoencephalography or ultrasonography (Horbar et al., 1983; Strauss & Fitz, 1980). Significant ventricular asymmetry in the absence of ventriculomegaly was reported by Achiron et al. (1997). In the majority of cases, the index sonogram showed that the left lateral ventricle was larger than the right one. Shen & Huang (1989), in an ultrasonographic examination of normal full term neonates found asymmetry of size between the right and left lateral ventricle. The most common finding of ventricular difference was asymmetry of occipital horn. The mode of delivery did not significantly influence the occurrence of ventricular asymmetry, indicating that asymmetry of the lateral ventricle is influenced by genetic factors or environmental events that occur during the growth of the brain and not by the pressure effect through the birth canal. In normal adults the left lateral ventricle is reported as wider than the right and the left posterior horn as longer (Petty, 1999). In a three-dimensional ultrasonographic study of ventricular volume in normal neonates, Ichihashi et al. (2005) reported the left ventricle larger than the right one, and that the lateral ventricular size became larger during the first two weeks after birth. Batton & Swails (1998), reported incidence of asymmetry of the lateral ventricles in VLBW infants (birth weight 500-1500gms) who did not have evidence of other intracranial pathology, and concluded that isolated ventricular asymmetry in VLBW infants is not uncommon, occurs much more frequently on the left side, and is associated with respiratory distress syndrome.

Cerebrospinal fluid (CSF) asymmetry was noted around the regions of grey matter asymmetry, particularly in the right hemisphere and most prominently in the right Sylvian fissure (Good et al., 2001).

Functional Asymmetries:

Functional asymmetry is one of the most fundamental characteristics of the brain and involves differences in the pattern of participation of right and left hemispheres in psychological functions and regulation of autonomic processes. The human brain is unique in the functional asymmetry that exists between its two hemispheres (Wada et al. 1975), and this asymmetry has been found in all age groups from the fetus to the adult (Wada et al. 1975; Chi et al. 1977). The increase in brain complexity seems to be linked to the expression of cerebral asymmetries (Hellige, 1993). There are several kinds of functional asymmetries: motor, sensory, autonomic, biochemical and psychological. Functional asymmetry is based on biochemical asymmetry characterized by an uneven distribution of neurotransmitters between paired structures of the brain.
The two hemispheres are specialized for distinct cognitive and behavioral functions. These functional asymmetries have been related to anatomical asymmetries of the cortex that are somewhat more subtle (Galaburda & LeMay, 1978; Toga & Thompson 2003). The left hemisphere is often related to learning, analytical and sequential processes, such as the execution and coordination of movements or language organization (syntax, decoding, producing), discrimination, categorizations and local dynamics, while the right side is linked to emotional systems, visuospatial processing, relational aspects and global dynamics. The left hemispheres subserve language functions, while the right hemisphere is specialized for processing of spatial relations and for emotional control (Springer & Deutsch 1997).

Anatomical studies have shown that hemispheric asymmetry is especially found in several distinct areas (Wada et al. 1975; Galaburda et al., 1978), and the structural asymmetries have frequently been associated with language lateralization (Geschwind & Levitsky, 1968; Price, 2000; Toga & Thompson, 2003). Likewise, functional asymmetries such as lateralized hand and foot preferences might be expected to correlate with brain structure (Amunts et al., 2000; Beaton, 1997; Moffat et al., 1998). The two hands are also almost anatomically perfect mirror images of each other, but are clearly asymmetrical with regard to function or physiology. The evolution of bipedalism freed the hands from participation in locomotion and allowed them to evolve new functions, such as feeding, food gathering, and tool using, and manipulating rather than simply reacting to the environment. The hands came to perform different functions, for example, in tool-making, for which one hand holds the material while the dominant hand shapes it. A clear majority of the population (90%) prefers the right hand for manual activities, with superior fine motor control and motor strength (Beaton et al., 2000; Corballis, 2003).

The right parieto-temporal system is directly activated during spatial discrimination and visuospatial analysis (Faillenot et al., 1999), as well as in detection and integration of sound movement (Griffiths et al., 1998). Females have relatively more developed grey matter in these areas (Nopoulos et al., 2000). The left frontoparietal structures (especially the supramarginal, parietal lobules) are involved in spatial orienting and “motor attention” (Griffin et al., 2001; Rushworth et al., 2001). Both superior parietal lobules are activated by contralateral finger movements during spatial selection and visuo-motor tasks (Shibata & Ioannides, 2001). Spatial behaviour, generally related to parietal systems, induces the activation of the right superior temporal areas (Karnath, 2001; Karnath et al., 2001). The left counterparts in modern humans represent a large portion of Wernicke’s area, leading to hypotheses about the possible coevolution of different hemispheric specializations. Some behaviours were more affected by right-hemisphere damage than by left-hemisphere damage (Bryden, 1988). There is some evidence that subject with left temporal lobe damage have deficits in the performance of verbal tasks compared to normal subjects and patients having undergone right temporal lobe damage (Frisik & Milner, 1991; Ribbler & Rauch, 1990). There is also evidence that subjects with right hemisphere lesion perform at lower levels than normal controls and subjects with left hemispheric lesions when performing a visual-spatial task (Ditunno & Mann, 1990; Warrington & James, 1967a).

Neuroimaging data have also pointed to functional asymmetries in amygdalar function. Several studies suggest that the right amygdala responds more to experientially learned or conditioned fearful stimuli, whereas the left amygdala appears more active during the perception of innately fear-related items such as photographs of threatening stimuli or fearful faces (Büchel et al., 1998; Dolan & Morris, 2000; Morris et al., 1998). Furmark et al., (1997) noted that regional cerebral blood flow in the right, but not the left, amygdala correlated with autonomic responses to averscively conditioned.

A study in newborns to determine the dynamic lateralization in the head turning after release from the midline and its relationship with obstetric variables showed that the right-sided head lateralization was significantly greater than the left-sided (Beuter et al., 2007). Hepper et al., (1998) observed that this lateralization starts its development in the prenatal stage, specifically from ten weeks gestational age. The findings agree with Rönnqvist et al. (1998) when studying head lateralization in newborns through Moro response, discovered a right-sided head preference in the ratio of 2 (right): 1 (left). They also found no evidences of association between type of delivery and head turning lateralization.

Functions such as speech, reading and facial recognition are asymmetrically located in the brain. Language is processed asymmetrically in the human brain, with the left hemisphere dominant compared with the right. This lateralization is functionally significant (Knecht et al., 2002), modality independent (Hickok et al., 1998; Grossi et al., 1996), and is associated not merely with the perception or production of utterances but with their meaning (Zahn et al. 2000; Thiel et al., 1998).

In a study by Domellöf et al. (2005), asymmetries in head turning were compared to those in leg movements during stepping and placing, with the latter also being related to differences in leg mass. The effects of an active versus an inactive state or condition were examined for all three behaviors. No overall lateral biases were found for head turning or for the first foot to move in stepping and placing, and there were no concordances among them; however, there was an asymmetry in that the left foot had shorter onset latency when compared to the right foot for both stepping and placing.
There are instances in which human motor behavior is also known to have asymmetric features (Maupas et al., 1999; VanZant et al., 2001; Childs et al., 2003). Sitting is an example of human motor behavior. Maupas et al (1999) found that there was asymmetry in knee flexion angles for more than one-half of all individuals while walking, and concluded that such asymmetry is normal and that asymmetry should be considered when working with both healthy and pathological individuals. Mobility of facial expression also exhibits facedness. (Smith et al., 2000) Most studies suggest that the left side of the face is more expressive of emotions (Sackeim et al., 1978; Asthana & Mandal, 1998; Indersmitten & Gur, 2003) Such a functional asymmetry in facial expression may have some relationship to the dimensional balance between the left and the right hemiface.

**Skeletal Asymmetries:**

Differences have been noted between or within body structures within an individual (intra-individual variation) with regard to the size and shape of the face & skull, spine, girdles and limb bones. Subtle facial directional asymmetry is present in healthy individuals (DeLeon, 2007; Ercan et al., 2008; Schaefer et al., 2006). A mild degree of asymmetry is common in the face of normal human individuals (Lu, 1965; Vig & Hewitt, 1975; Shah & Joshi, 1978 Alavi, Begole & Schneider, 1988; Peck et al., 1991; Pirttiniemi, 1992; Ferrario et al., 1993a; Ferrario et al., 1993c). The two sides of face showed significant differences in shape, but no differences in size. (Ferrario et al., 1995) The degree of asymmetry is obviously higher in unhealthy individuals, where irregular development of skeletal, dental and soft tissues can characteristically contribute to clinically discernible imbalances (Williamson & Simmons, 1979; Alavi et al., 1988; Pirttiniemi et al., 1990; Schmid et al., 1991; Pirttiniemi, 1992). Reports have suggested that facial asymmetry is likely to exhibit laterality (Shah & Joshi, 1978; Burke, 1979; Koff et al., 1981. Farkas & Cheung, 1981; Ferrario et al., 1993a; Vig & Hewitt, 1975; Chebib & Chamma, 1981; Haraguchi et al., 2002; Severt & Proffitt, 1997). In all investigations a significant facial asymmetry has been demonstrated even in aesthetically pleasing faces, but no agreement exists about the side of dominance (Woo, 1931; Lu, 1965; Vig & Hewitt, 1975; Shah & Joshi, 1978; Williamson & Simmons, 1979; Alavi et al., 1988; Pirttiniemi et al., 1990; Peck et al., 1991; Schmid et al., 1991; Melnik, 1992; Pirttiniemi, 1992; Ferrario et al., 1993 d).

Most examinations on face asymmetry proved that domination of the left side is more common in the human population (Lanzieri et al., 1988). Although Vig & Hewitt (1975) found in their radiographic investigation that the cranial base and maxillary regions were significantly larger on the left side, Shah & Joshi (1978) stated that the total facial structure was larger on the right side. Woo (1931), working on skulls, found that the right frontal and parietal bones were larger than the left, but that the left malar bone was predominant. Gundara & Zivanovic (1968), reported asymmetry in 98% of the skulls and was observed mainly in parietal and occipital regions. Study by Ginsberg, Pret, Chen & Elster (1994) by comparing CT images of the skull reported asymmetry of the Valesius foramen. Asymmetry of the ovale and spinous foramina in the size, shape and distance from the midline was stated by Teul et al. (2002). The distance of both foramina from the anterior margin of the foramen magnum and the midline is shorter on the left side, showing the domination of the right half of the skull.

In the photographic study by Ferrario et al. (1993 d) the lower part of the face was dominant on the right side in both men and women, while Peck et al. (1991) found larger right-side structures but the difference was not statistically significant. Melnik (1992) stated that the side of facial dominance was a function of age: while at 6 y of age the left side was the larger, at 16 y the right side was dominant. Haraguchi (2008) found a consistent tendency for dominance of the right hemiface. As the growth stage proceeds, however, right-sided dominance becomes less frequent, whereas left-side dominance becomes more frequent. Laterality in the normal asymmetry of the face is consistently found in Japanese orthodontic patients. The right-sided dominance of the face was independent of sex, age, and skeletal jaw relationships. In this regard, the proportion of subjects with a wider right hemiface was larger at earlier ages than at later ages, while the proportion of subjects with a wider left hemiface was larger at later ages than earlier. A mild degree of facial asymmetry, may be affected by handedness (1997; Pirilä-Parkkinen et al., 2001), is common in humans (Ferrario et al., 1993, 1995; Haraguchi et al., 2002). Osborn & Homberger, (2009, 2010) showed that in right handed individuals, the humerus diameter, mastoid process width, and rise of the superior nuchal line were more often larger on the right side, while the clavicle length and scapular breadth were so on the left side.

Interindividual and intraindividual variations in the size and shape of the frontal sinus have been reported (Quatrehomme et al., 1996). They vary markedly in size and depth and are often asymmetrical. Because the left and right frontal sinuses develop independently, a significant asymmetry between these sinuses can arise in the same individual (Levine & Clemente, 2003) Asymmetry for the frontal sinuses of both sides is a rule because of unequal resorption of the diploe during sinus development (Yoshino et al., 1987). Taniguchi et al. (2003) reported frontal sinus asymmetry in human autopsies with left hand dominant in 31.2% and right hand dominant asymmetry in 25.4%.
Human bodies and human backs are structurally asymmetric. Harrison & Robinette (2002) demonstrated asymmetry in left-right body dimensions for anatomic structures such as the height of the trochanters (hip) above the seated surface and seated elbow height. Dickson et al., (1984) reported that asymmetry in the structure of the spine in one plane is normal, becoming pathological only when it is asymmetric in two orthogonal planes. Although the prevalence of pelvic asymmetry has been reported in patients with back pain to be 24-91%, its prevalence in the general population is not known. Pelvic asymmetry can also be observed in healthy subjects with no evidence of any dysfunction (All-Eisa et al., 2004, 2006). Saulicz et al. (2001) demonstrated that pelvic asymmetry was present in 67.3% of a healthy group (aged 18 to 39 years) with no pelvic or low back pain (Saulicz et al., 2001). In a total of 323 consecutive CT scans of the pelvis/abdomen, pelvic asymmetry of >5 mm was uncommon and ranged in magnitude from −11 mm to 7 mm (right pelvis (mm) – left pelvis (mm)) (Badii, et al., 2003). Akman et al., (2008) found that measurements of posterior-lateral ala breadths and maximum auricular surface height, were identified statistically significant larger in the left side but little was found greater in the right side. Johns Hopkins Children's Center researchers (2011) have discovered that most children with severe cerebral palsy have starkly asymmetric pelvic bones.

Human clavicular asymmetry is significantly left-biased in length and right-biased in diaphyseal breadth. (Parsons, 1916; Schultz, 1937; Ray, 1959; Huggare & Houghton, 1994; Mays et al., 1999; Voisin, 2001; Auerbach & Raxter, 2008). In contrast, mean humeral directional asymmetries are all right-biased among humans.

The long bones of human skeleton usually show asymmetries of length (White & Folkens, 2005). The asymmetry between the bones of the upper limbs has been reported in earlier studies (Arnold, 1884; Gennadis, 1858; Warren, 1897). It exists, with little differences, in all races (Schultz, 1937; Schell et al., 1985). The difference is significantly greater in males than in females (Schultz, 1937; Ruff & Jones, 1981; Hiramoto, 1993) and was estimated as high as 4.1mm by Schultz (1937). It tends to occur more in bigger men (Stirland, 1993). It decreases with age (Singh, 1971; Pande & Singh, 1971; Ruff & Jones, 1981; Stirland, 1993; Scheuer & Black, 2007). The upper limb bone dimensions, especially in length (Hiramoto, 1993; and diaphyseal breadth (Le May, 1992; Papaloucas et al., 2008) are greater than the bones of the lower limb. The weights and lengths of right and left bones of each pair, from 105 human skeletons from Asia, were studied by Latimer & Lowrance (1965). All of the long bones of the upper limb were heavier and longer on the right side. The left femur was heavier and longer. The right tibia and fibula were heavier while the left tibia and right fibula were longer. The right scapula was heavier and the os coxae, clavicle and the bones of the hand and foot were heavier on the left side. Generally, the left bones are more variable in weight and length. The upper extremity and its individual bones manifest more asymmetry than the lower. The proximal bone of upper and lower extremities and the scapula and os coxae show a greater degree of asymmetry in weight than the the more distal bones.

Studies of lateral asymmetry of the legs have confirmed that the left leg is heavier than the right but the results of differences in length are not uniform (Latimer & Lowrance 1965; Singh 1970). Ruff and Hayes studied the asymmetry in the shape of the femur. They determined that the left femur is stronger, particularly in women but they did not find a difference in length (Ruff, 1992). After statistical analysis on 166 South African Negroes thigh bones, Macho (1991) came to the conclusion that on average the left leg was stronger and in most people, regardless of right- or left-handedness, was the supporting leg while the right was used for other functions. Ćuk et al. (2001) performed analysis of lateral asymmetry on medieval skeletons and their results confirm the presence of oriented asymmetry more prominent in the arms than the legs. The average lateral asymmetry in the arms was to the right, in the legs to the left. By far the most asymmetric bone was the humerus where almost all the parameters were highly significant. “Crossed symmetry” patterns between upper and lower limbs were supported by Auerbach & Ruff (2004). Sexual dimorphism in asymmetry is present in some dimensions, especially those of the upper limb, and may implicate fundamental differences in both behavior and bone growth between males and females. Females have more asymmetric and right-biased upper limb maximum lengths, while males have greater humeral diaphyseal and head breadth percentage directional asymmetries (%Das). The lower limb demonstrates little sexual dimorphism in asymmetry. Industrial groups exhibit relatively less asymmetry than pre-industrial humans and less dimorphism in asymmetry. A mixture of influences from both genetic and behavioral factors is implicated as the source of these patterns (Auerbach & Ruff, 2006). Finally, more recent populations show a diminishing of the directionality and magnitude of asymmetry and sexual dimorphism in asymmetry, probably reflecting changes in exogenous factors, such as division of labor (Auerbach & Ruff, 2006).

The dominance of the lower extremity is less marked than that of the upper. The dominant leg is expressed by the stronger tibia usually on the opposite side of the dominant arm. The stronger development of the left femur as supportive limb is characteristic of both right- and left-handers Ćuk et al. (2001). Thus, right-handers usually have a dominant left leg, left-handers a dominant right. In the majority of people the supportive leg, without regard to hand dominance, is the left as shown by the greater development of the femurs in both right and left-handers. Singh & Mohaty (2005) have reported that there were higher incidences of heavier and longer bones on the right side, suggesting right dominance. The absolute weight and length of right extremity bones
were also more. The tibia and fibula were best qualified as pointers towards right dominance in terms of both weight and length. The right dominance was considered a congenital phenomenon guided by contralateral dominant left cerebral hemisphere. The right dominance was significant for individual bones like female femur, tibia and fibula. The asymmetry was less pronounced in case of tarsals and metatarsals. However, for hip bones, there was higher rate of heavier bones on left side, but the difference was not statistically significant. The authors observed preponderance of heavier bones on the right side and the asymmetry was more pronounced in the upper extremity than the lower extremity.

Structural asymmetry in fetal metatarsal bones on the right and left side was reported by Gawlikowska et al. (2007). In the younger group, the character of the asymmetry fluctuated. A clear one-sided domination in all metatarsal bones appeared only in the oldest group (over 26 gestational weeks). These results demonstrate that such asymmetry forms and matures during ontogenesis, similarly to other systems and organs (Gawlikowska et al. 2007).

Variation and asymmetry was also reported by Manning et al. (1998a) in the ratio of second to fourth digit (2D:4D) in hand. Men tended to have a lower 2D:4D ratio than women and in men 2D:4D was negatively related to sperm numbers and testosterone levels and positively related to oestrogen and LH levels. In women 2D:4D was positively correlated with oestrogen and LH. They also found that all relationships were stronger for the 2D:4D ratio of the right hand compared to that of the left. Low 2D:4D ratios in the right hand correlate with a reduction in left-hand performance times (Manning et al., 2000). Left-handed individuals in the ‘normal’ population have also been shown to have equivalent but reversed asymmetry in metacarpal dimensions compared to right-handed individuals (Roy et al., 1994). Singh (1979) showed bilateral asymmetry in the direction and degree of tortion in metatarsal bones. This was most evident in the case of first metacarpal. Garn et al., (1975) have found that adult bone-to-bone ratios of the phalanges are established by 13 weeks.

**Vascular Asymmetries:**

Several variations and asymmetries are reported in the vascular pattern of human body. The common carotid artery bifurcation is most commonly located between the C3-4 and C4-5 levels, but it may be at any cervical level (Gray, 1980). Osborn (1999) showed that the normal common carotid artery bifurcation is at or near the level of the thyroid cartilage (approximately C4), but bifurcation may occur as high as C1 or as low as T2. Lo et al. (2006) found that the common carotid artery bifurcation point was at the level of the body of the hyoid bone in 40% of the cases, and the level of the bifurcation was asymmetrical between the left and right sides. Gulsen et al. (2009) have reported a case in which the bifurcation of the common carotid artery was located between the body of the C6 and C7 on the right side and between the body of the C5 and C6 on the left side. Smith & Larsen (1979) studied bilateral carotid angiograms of the neck in 100 consecutive adult patients and showed the bifurcation of the left common carotid artery located cranial to the right in 50% of the cases, while the right bifurcation was higher in 22%. The origin of the internal carotid artery was also asymmetrical; at the dorsal or dorsolateral aspect of the common carotid artery in 82% on the right side and in 94% on the left, while a dorsomedial or medial origin was found in 18% on the right side and in 6% on the left.

In a case-control study done to determine whether an asymmetry of size of the intracranial internal carotid artery (ICA) on 3D time-of-flight MR angiography (MRA) is predictive of a high-grade cervical ICA stenosis, Naggara et al., (2008) showed that intracranial ICA was predictive of a ≥70% cervical ICA stenosis with a high degree of confidence.

Asymmetry of size between vertebral arteries (VAs) is the rule, and a marked size difference may be present in up to 15% of healthy subjects (Stopford, 1915). Asymmetry of the intracranial parts of the VAs is common (95%) (Kazui et al. 1989). It is known that left VA is usually larger than the right one (Paksoy et al., 2004; Jeng & Yip, 2004; Kazui et al., 1989). The left vertebral artery is dominant in approximately 50%; the right in 25% and only in the remaining quarter of cases are the two vertebral arteries of similar caliber (Cloud & Markus, 2003). Morović et al., (2007) reported left VA dominant in 57% in both men and women. The VA hypoplasia was present in 2.34%, asymmetry in 15% with left VA dominant in 64% (Lovrenciċ-Huzjan et al., 1999). In up to 15% of the healthy population, one vertebral artery is atretic (<2 mm diameter) and makes little contribution to basilar artery flow. Lesser degrees of asymmetry are also frequent. It has been also concluded that VA asymmetry leads to basilar deviation (Kazui, et al., 1989). Deviation is usually detected towards the larger VA, to the opposite side. Uzmansel et al. (2009) reported the deviation of the basilar artery to the left, towards the larger right VA.). The diameter of the vertebral artery ranged from 2.3 mm to 7.4 mm (average 4.2 mm). The dimensions of the left side artery ranged from 2.3 mm to 4.5 mm whilst that on the right side artery ranged from 4.1 mm to 7.4 mm. In one specimen, there was a marked difference in the size of the artery on the left and right side, the artery on the left side being significantly hypoplastic (Cacciola et al., 2004).

In many patients, marked asymmetry in relative vertebral artery size and position, and in the size relative to the transverse foramen (with the vertebral artery occupying 8-85% of the foramen) was observed. This asymmetry would often vary markedly from level to level within the same patient. Vertebral artery size and position in the transverse foramina vary markedly in normal young subjects. These normal variations must be
considered when evaluating vertebral arteries. (Sanelli et al., 2002). Madawi et al. (1997) found frequent asymmetry in the grooves for the vertebral artery in 50 dry specimens of the second cervical vertebra (C2). In 11 specimens one of the grooves was deep enough to reduce the internal height of the lateral mass at the point of fixation to ≥1.1 mm, and the width of the pedicle on the inferior surface of C2 to ≥2 mm.

Henriquez-Pino et al., (1993) reported asymmetry in the relation of the internal thoracic artery to the phrenic nerve. A study by Toni et al., (2003), on the anatomy of human thyroid arteries in Caucasians and Asians showed that the presence and site of origin of the superior (STA), inferior (ITA), and lowest accessory (IMA) are influenced by the anthropological group and reported asymmetry between the right and the left sides. Eisen et al., (2006) found that the femoral and radial arteries were often asymmetric. The right femoral artery was usually larger than the left. Asymmetry has also been reported in the size and position of jugular bulb. The right jugular bulb is usually larger than the left and it may reach above the posterior semicircular canal (Beek & Pameijer 2011).

The sizes of the lateral sinuses are often asymmetric with the left transverse sinus being smaller (or even absent) than the right one (Sajjad 2006). An asymmetrical flow with the larger blood volume from the superior sagittal sinus flowing into the right transverse has been reported (Navsa & Kramer, 1998). This asymmetry is probably a direct consequence of the petalia pattern, and it is clearly individual-specific. The patterns at the confluence of sinuses, with all the extreme variability presented, could be merely a secondary product of cerebral asymmetries (Grimaud-Harvé, 1997). Venous angiography of the cavernous and inferior petrosal sinuses has shown variation in the venous drainage of the cavernous sinus. Venous drainage was bilaterally symmetric in 14 patients (61%) and asymmetric in 9 (39%). The most common asymmetric pattern was for blood from both cavernous sinuses to drain into the right inferior petrosal sinus, with no significant drainage into the left (Mamelak et al., 1996).

Genital Asymmetries:

With regard to genital asymmetry, Chang et al., (1960) found that the left testicle is lower in right-handers, whereas the opposite pattern occurs in left-handers. It was also reported that the right testicle is larger than the left (Chang et al., 1960; Short, 1984; Mittwoch, 1988; Kimura, 1993). In human fetuses, the right testicle seems to develop more quickly than the left (Mittwoch, 1975, 1977; Mittwoch & Kirk, 1975). Testicular asymmetry (e.g. left testicle hanging lower) has been attributed to more well-developed and greater flexion of the muscles on one side of the lower abdomen relative to the other side (Chang et al., 1960) and/or the different length, that angle and source of the blood vessels supplying the two testicles (Antliff & Shampo, 1959). Interestingly, varicoceles, when they occur in men, are also usually left-sided, a pattern that has been attributed to the characteristics of the blood vessels supplying the two testicles (Sherins & Howards, 1986). Given that genital asymmetry seems to be related to handedness, such measures may also be used as indicators of cerebral asymmetry, and thus, perhaps, related to patterns of cognitive skills. Differences in testicular size have indeed been related to cognitive skills, where, for example, men with a larger right testicle were found to perform better on certain spatial tasks than men with a larger left testicle (Kimura, 1994).

Most men reported some degree of lateral asymmetry in their flaccid penis and in their testicles; less asymmetry was reported for their erect penis. The asymmetry typically occurred in the left direction, and this pattern occurred in both right- and non-right-handers. However, this ‘leftward’ pattern was significantly less pronounced in non-right-handers (Bogaert 1997; Ben-Ari et al., 1985) observed that normal male newborns, when they have some lateral asymmetry of the shaft of their penis, are more likely to have a left rather than a right inclination. Finally, Kimura (1992), in a preliminary report, indicated that 67% of 111 university men reported that they had a leftward inclination, of their flaccid penis. The source of the penile deviation is less well considered. However, a number of factors may be important, including possible slight differences in the relative sizes of the right and left corpora cavernosa, more well-developed and increased flexion of the muscles on one side of the abdomen relative to the other (Chang et al., 1960) or even possible local effects of surgery in some men (e.g. circumcision).

In females, there are large inter-individual differences in size and asymmetry of breasts and this could be indicative of differences in developmental stability, and possibly disease predisposition. Breast volume FA, as measured from mammograms, is related to several of the known risk factors for breast cancer (Manning et al., 1996), and patients with diagnosed breast cancer have higher breast volume FA measured from mammography than age-matched healthy women (Scutt et al., 1997). Breast asymmetry is likely to be a predictor of, rather than the effect of breast cancer. (Scutt et al., 1997). Breast asymmetry was greater in the healthy women who subsequently developed breast cancer than those who remained disease free (Scutt et al., 2006). Asymmetrical breasts could prove to be reliable indicators of future breast disease in women and this factor should be considered in a woman's risk profile.

In human females, higher levels of breast asymmetry are associated with lowered fecundity (Møller et al., 1995; Manning et al., 1996). Manning et al. (1996) showed an association between breast asymmetry and delayed fecundity in human females. Livshits & Kobyliansky (1991) found that high FA in parents predicted a
higher number of pre-term (and therefore less viable) infants. Möller and colleagues (1995) found that large breasts had more FA than small breasts, breast FA was higher in nulliparous women, and that breast FA was a predictor of fecundity.

Genital asymmetry also varied, to a small degree, as a function of handedness. Like right-handers, nonright-handers were more likely to have a left inclination than a right inclination, but this trend was not as pronounced. These data are consistent with previous observations that nonright-handers may be less pronounced in some lateral body asymmetry relative to right-handers (Garn et al., 1976; Plato & Woods, 1980).

Establishing a relationship between handedness and genital/sexual organ asymmetry may also be important because of sexual/reproductive health issues. Cancer of the breast in women and testicular cancer in men may reflect lateral bodily asymmetry, where the larger breast or testicle may be, on average, more likely to be affected by cancer than the smaller one (Spitz et al., 1991). It has also been reported that handedness may influence the laterality of breast cancer (Hsieh & Trichopoulos, 1991).

**Etiology of Body Asymmetries:**

Asymmetry can be of genetic or nongenetic origin. Among the former type are the fundamental forms for which the signals present in the inherited genetic constitution produce definite right-left differences. The nongenetic forms of asymmetry can be determined by the influence exerted by the external environment, or they may be due to random developmental differences in the internal environment of the two halves of the body. In the case of some forms of asymmetry, the appearance of right-left differences is probably due to a combination of genetic and nongenetic influences; that is, the responsible genes display incomplete penetrance or irregular expressivity. The origin of lateralization involves both ontogenetic and phylogenetic factors (Babcock, 1993). In humans, some anatomical or behavioural asymmetries are observable at birth or even in foetal stages. Speech and language functions, however, seem to become increasingly lateralized through early ontogeny, reaching full lateralization about the time of puberty.

**Genes:**

A variety of genetic studies, including twin, family, adoption, and cross-fostering studies, demonstrated that handedness in humans has a significant genetic component (Arnold, 1844; Gennadis, 1858; Schultz, 1926, 1937; Chamberlain, 1928; Pande & Singh 1971; Singh 1971; Annett, 1974; Carter et al., 1976; Hicks & Hinsborne 1976; Longstreth, 1980; McManus, 1991; Vettel et al., 1995; Scheuer & Black, 2007). Combined genetic – MRI studies suggest that heredity plays a central role in shaping the perisylvian cortex; gray matter volumes seem to be highlyheritable (Posthuma et al., 2002; Thompson et al., 2001) whereas gyral and sulcal patterns appear much less heritable (Lohmann et al., 2008). A nice genetic model for left- and right-handedness has been put forward by McManus (2002). He assumed that there are just two genes controlling handedness, a dextral gene, D, and a chance gene C. People with two copies of the D gene, who are thus DD, will always be right handed; those who are CC will be left or right 50% of the time and CD individuals have a 25% chance of being left-handed.

There is evidence that homologous areas of the left and right hemispheres mature at different rates, beginning in utero and continuing through at least the first few years of human life. At least in humans, certain areas of the right hemisphere develop earlier in utero than do homologous areas of the left hemisphere, leading to the suggestion that the earlier developing right hemisphere is initially more influenced by the sort of impoverished information that the developing brain encounters before and for a short time after birth (Hellige, 1993, 1995, 2006). Sun et al. (2005), by applying serial analysis of gene expression (SAGE), measured gene expression levels between the left and right hemispheres in early (12- to 14-week-old) fetal human brains, during periods of neuronal proliferation and migration, and later (at 19 weeks), suggesting that human cortical asymmetry is accompanied by early, marked transcriptional asymmetries and human left-right specialization reflects asymmetric cortical development at early stages. They identified and verified 27 differentially expressed genes, which suggests that human cortical asymmetry is accompanied by early, marked transcriptional asymmetries. *LMO4* is consistently more highly expressed in the right perisylvian human cerebral cortex than in the left and is essential for cortical development in mice, suggesting that human left-right specialization reflects asymmetric cortical development at early stages. Abrahams et al. (2007) performed a genome-wide analysis of human cerebral patterning during midgestation, a critical epoch in cortical regionalization. A total of 345 genes were identified as differentially expressed between superior temporal gyrus and the remaining cerebral cortex.

**Hormones:**

Prenatal testosterone has been implicated as an important factor in the development of extragenital sexual dimorphism including the differentiation of the nervous system (Bardin & Caterall, 1981; McEwen, 1981; MacLusky & Naftolin, 1981). One such dimorphism may be seen in the expression of hand preferences (Geschwind & Behan, 1982; Geschwind & Galaburda, 1985; Hassler & Gupta, 1993). Geschwind & Galaburda (1985) have hypothesized that testosterone may slow growth within some areas of the left hemisphere and
promote growth of certain areas in the right hemisphere. Such a process may mean that high levels of testosterone in utero would be associated with left handedness and this left-preference could be seen in higher frequencies in males. Geschwind & Galaburda (1985) have also implicated testosterone in the aetiology of autism, dyslexia, migraine, stammering, autoimmune disease, sexual preferences, and spatial, language, music, and mathematical abilities. Sex hormones have powerful neuromodulatory properties that dynamically change the functional brain organization (i.e., hemispheric asymmetries and interhemispheric interaction) and cognitive behavior not only during prenatal development but throughout life. Majority of studies suggest that gonadal steroid hormones affect functional development during early ontogenesis (Murphy et al., 1994) and maybe also lower the 2D:4D ratio of the right hand (Manning et al., 1998b).

Moreover, these studies suggest that genetic factors can change the normal hormonal environment which eventually affects hemispheric asymmetries as epigenetic factors during ontogenesis. Hormones appear to play a large role in mediating bodily asymmetry, and phenotypic sex is related in systematic ways to cerebral asymmetry (de Courten-Myers, 1999; Frederikse et al., 1999; Kulynych et al., 1994; Moffat et al., 1998). Likewise, functional asymmetries such as lateralized hand and foot preferences might be expected to correlate with brain structure (Amunts et al., 2000; Beaton, 1997; Moffat et al., 1998).

Environmental Factors:

Ability to changes is one of the important properties of a living organism which is well visible in the course of individual life. Degree of asymmetry, as a constant property in the process of ontogenesis where changes in functional, dynamic and morphological asymmetry appearing with age (Wolanski, 1972). During childhood, the shape of the body continuously changes because of the different rates of growth of different parts. The gross changes in bodily proportions during growth in the human have been analyzed (Medawar, 1944). The degree of asymmetry reflects the degree of force exerted onto the right or left limb whereas the particular bone site showing the asymmetry indicates the kind of force exerted (Cuk et al., 2001).

Singh & Singh (2007) used the anthropometric methods to find out the level and range of bilateral asymmetry of upper limb in relation to habitual physical activity. Their results supported the earlier findings that most asymmetric trait of human body is hand muscular strength, which further depends on the mass of working muscles, degree of their development and the conditional reflexes which regulate and co-ordinate the movements (Gusieva, 1964), and the maximum bilateral differences in hand occurred in mechanics, metal workers and weavers (Malinowski, 1975). Vigorous training might change bone dimensions if this was undertaken before closure of the epiphyses has been completed (Tittle & Wutschker, 1992; Haapasalo et al., 2000). Asymmetry is also influenced by mechanical loading or disuse of a limb (Singh, 1971; Steele and Mays, 1995). Use of dominant limb in athletes results in greater asymmetry (Ruff & Jones, 1981), while the activities involving non-dominant limb may change the asymmetry (Stirland, 1993) between the right and left humerus. Activities involving both limbs equally may result in lack of asymmetry (Rule, 1982; Stirland, 1993). This hypothesis was strongly supported by observations of greatly increased asymmetry between the playing and nonplayin games of racquetball and tennis athletes (Jones et al., 1977; Krahl et al., 1994; Ruff et al., 1994; Kontulainen et al., 2001, 2002; Bass et al., 2002), as well as between normal and mechanically compromised (i.e., paralyzed or otherwise mechanically restricted) limbs (Biewener & Bertram, 1993; Trinkaus et al., 1994).

White et al., (1994) and Steele & Mays (1995) related the asymmetry between the right and left limb to the brain asymmetry and suggested that because the cerebral hemispheres control the contralateral side of the body, and the left hemisphere is larger than the right and functionally superior (Vettivel et al., 1995), it shows its dominance influence on the right limbs.

The asymmetry of limbs in also reported in fetuses (Schultz, 1926; Le May, 1992). Pande & Singh (1971) studied in fetuses and found the total muscle and bone weight greater on the right side, proving the inheritance of stronger and heavier muscles and bones in the dominant limb. Trauma or toxins in fetal or early life may exhibit an influence on the asymmetry (Pande & Singh, 1971; Le May, 1992). Protein deficiency diminishes the asymmetry as reported by Steyn & Iscan (1999) and Mall et al. (2001). Though, right dominance is considered as congenital phenomenon (Pande & Singh, 1971; Taylor JR & Halliday, 1977), the dominance pattern could also be influenced by postnatal adaptation and physical work (Prives, 1960; Krishan, 2008) and can be enhanced or reduced according to individual’s habits and activities, age, nutrition, overuse or disuse of the limb (Papaloucas et al. 2008). Industrial groups exhibit relatively less asymmetry than pre-industrial humans and less dimorphism in asymmetry. A mixture of influences from both genetic and behavioral factors is implicated as the source of these patterns (Auerbach & Ruff, 2006).

Most studies on the possible causes of facial laterality concluded that environmental influences were the most likely cause. Habitual chewing on one side has been reported to lead to increased skeletal development on the ipsilateral side (Shah & Joshi 1978) Others have also discussed the possibility that such laterality is simply a response of functional adaptation to asymmetrical masticatory activity (Vig & Hewitt 1975). Pirttiniemi (1998) suggested that the normal asymmetry of the human face primarily originated from brain and skull base asymmetry (Pirttiniemi1998). It is also reported that children prenatally exposed to alcohol with a Fetal Alcohol
Syndrome (FAS) diagnosis tend to have stronger directional asymmetry than the children in the respective nonexposed control groups (Klingenberg et al. 2010). Sowell et al. (2002) reported that individuals with severe prenatal alcohol exposure have reduced asymmetry of the cortical surface and gray matter density.

The hypothesis that bilateral asymmetry have a genetic basis and are influenced by the intrauterine environment is supported by several studies (Vig & Hewitt, 1974; Bishara et al., 1994; Auerbach & Ruff, 2006; Sengupta & Karmaker 2006; Chia et al., 2008).

Geschwind et al., (2002) examined the volumes of left and right cerebral cortex in a large cohort of aging identical and fraternal twins and indicated that these right-hemisphere structures are more genetically determined than those on the left, and the left hemisphere is more susceptible to environmental factors than the right hemisphere. Because the majority of these twins’ lives have been spent apart from one another, these high heritabilities suggest that genetic background plays a larger role than environmental influences in the changes in brain structure that occur with aging.

An organism faces a variety of challenges from its environment during ontogeny. These genetic and external perturbations in the environment leave enduring signs on the adult body. For example, small deviations from perfect symmetry in bilateral traits are highly correlated with the amount of stress experienced during development (Siegel & Smookler, 1973; Siegel et al., 1977; Mooney et al., 1985). Adaptive development requires the organism to resist genetic and environmental stresses that disrupt the genetic plan for growth, a buffering capacity termed developmental stability (Thoma et al., 2002). Individuals are presumably buffered against such developmental insults by employing homeostatic mechanisms to produce the ideal phenotype (Clarke & McKenzie, 1992). Developmental instability is revealed by fluctuating asymmetry (FA), thus, fluctuating asymmetry is often used as a proxy to quantify developmental stressors and explore the effects of these developmental insults on individuals’ health, fitness, and behavior. The effect of developmental perturbations on an organism’s FA level appears to be trait-, sex-, and stressor-specific and dependent on the developmental stage of the individual (Hallgrimson et al., 2003; Badyae et al., 2005; Ivanovic & Kalezic, 2005). One way to carefully assess how various stressors affect morphology is to investigate concomitant physiological changes in the body. For example, human experience elevated steroid hormone concentrations, namely glucocorticoids in response to stress. Glucocorticoids in turn determine how body to effectively cope with the stressors. These influences may not only affect immediate survival, but future growth, health, and reproduction (Handa et al., 1994; Ferin, 1999; Viau, 2002; Viau et al., 2005; Kudielka & Kirschbaum., 2005), all implicated as correlates of FA (Knierim et al., 2007). In addition, sex steroid hormones, namely androgens and estrogens are in part responsible for growth and reproduction (Kudielka & Kirschbaum, 2005), and for the observed sex differences in response to stress (Kudielka & Kirschbaum, 2005; Maclusky & Naftolin 1981; McEwen, 1981; Migeon & Wisniewski, 1998). Several studies also linked androgens and estrogens to FA (Cunningham, 2000; Manning et al., 1997).

Clinical Implications:

Jack et al., (1995) highlighted the relevance of statistically characterizing volumetric measurement values in normal individuals. Specifying the range of normal values allows for greater sensitivity and specificity in clinical measurement and decision-making (O’Brien & Dyck, 1995). Valid normative volumetric information is essential for determining structural volume loss and changes in left–right asymmetry among patients. The presence of asymmetrical volumes in structures where symmetry is expected or the absence of asymmetry in structures where asymmetry is expected may be indicative of pathological processes and could provide insights into the biology of neuropsychiatric illnesses (Wang et al., 2001). As more and more data are accumulated with neuroimaging techniques like fMRI and PET, it has become more and more apparent that abnormal brain structure is evident in children diagnosed with different developmental disorders, such as autism, ADHD, and dyslexia.

Brain Asymmetries:

The two cerebral hemispheres are specialized for different functions. The discovery of anatomic asymmetries in the brain has given new light to our understanding of the cognitive differences between the left and right hemispheres (Galaburda & Rosen, 2006).

The differences in asymmetry of the anterior cingulate region seem to correspond with the behavioral style as subjects with a larger right anterior region described themselves as experiencing greater worry about possible problems, fearfulness in the face of uncertainty, shyness with strangers, and fatigability.

Evidence has been provided that asymmetry of the prefrontal cortex is associated with affective behavior and dysbehavior. Its relationship with aspects of the adolescents’ brain structure was investigated in a sample of 137 early adolescents (Whittle et al., 2008). Affective behavior was assessed during observations of parent–child interactions. The authors found male-specific associations between the volume of prefrontal structures and affective behavior, with decreased leftward anterior paralimbic cortex volume asymmetry associated with
increased duration of aggressive behavior, and decreased leftward orbitofrontal cortex volume asymmetry associated with increased reciprocity of dysphoric behavior (Whittle et al., 2008).

The hippocampus and amygdala are of particular interest, with numerous studies focusing on the volumetric measurement of these structures in a variety of clinical conditions. In temporal lobe epilepsy (TLE), for example, hippocampal and amygdala volumetric measurements can provide an index of mesial temporal sclerosis that is useful for seizure onset lateralization, surgical decision-making, and outcome prediction after surgical resection (Breier et al., 1996; Gilmore et al., 1995; Radhakrishnan et al., 1998; Salanova et al., 1999; Watson et al., 1997).

The relevance of hippocampal and amygdala volumes has also been investigated in schizophrenia, with several meta-analyses suggesting that schizophrenia is associated with bilateral volume reductions in both structures (Lawrie & Abukmeil, 1998; Nelson et al., 1998).

Reduced hippocampal volumes have been associated with mild cognitive impairment, thought to be a transitional state between normal aging and Alzheimer’s disease (AD) (Jack et al., 1997, 1999; Petersen et al., 2001), and measurement of hippocampal and amygdala volumes has been shown to improve the sensitivity of early AD diagnosis (Dickerson et al., 2001; Galton et al., 2001; Krasuski et al., 1998; Laakso et al., 1998). Experiments that investigate temporal changes of hippocampal asymmetry in healthy controls have shown that it tends to decrease over time; this pattern is distinct from the one in Alzheimer disease, where asymmetry tends to increase over time (Shi et al., 2007).

Damage to the right amygdala has been observed to produce a more global deficit in electrodermal responses than damage to the left amygdala (Gläscher & Adolphs, 2003; Weike et al., 2005), reflecting an asymmetry in global autonomic control. Data suggest that many of the cognitive processes and physiological responses that are symptomatic of PTSD are preferentially mediated by the right amygdala. These findings suggest that there is an asymmetry in the importance of the right and left amygdala in the development of post traumatic stress disorder (PTSD). Whereas both amygdalae may contribute to the expression of fear conditioning, the right amygdala would be predicted to play a more critical role in mediating the larger constellation of symptoms associated with PTSD. The symptoms of PTSD may arise in full even in the absence of the left amygdale (Smith et al., 2008). Using electronic databases, Woon & Hedges (2009) found nine studies comparing amygdala volumes in adult subjects with PTSD with amygdala volumes in comparison subjects (participants unexposed to trauma and participants exposed to trauma but without PTSD). Results showed no significant differences in amygdala volumes between the groups. Within each group, the right amygdala was significantly larger than the left, indicating an asymmetrically lateralized amygdala volume that is preserved in trauma exposure and in PTSD.

Schizophrenia. Areas in the left temporal lobe, overlapping with the planum temporale and Wernicke’s regions show structural abnormalities in both schizophrenia and dyslexia. Reduced asymmetry of the cortical surface area of the planum temporale was reported in brains of patients with schizophrenia (Chance et al., 2008). The neuronal density, size, and shape analyzed in Brodmann’s areas 9 and 10 in schizophrenia patients’ brains showed a larger density of neurons in the right as compared to the left hemisphere: the reversed pattern of what is seen in control brains (Cullen et al., 2006). Nakamura et al. (2007) reported significantly different distribution of the orbitofrontal sulcogyral pattern in schizophrenics as compared to controls, the distribution differed significantly from controls, possibly reflecting a neurodevelopmental aberration in schizophrenia. Moreover, the asymmetry observed in controls was not present in schizophrenia.

Stronger directional asymmetry is often associated with conditions that disrupt normal craniofacial development, such as cleft lip and palate (Bock and Bowman, 2006), deformational plagiocephaly, or craniosynostosis (Netherway et al., 2006). Changed patterns of directional asymmetry have been reported among individuals diagnosed with disorders in which facial changes may be a secondary consequence of abnormal brain development, such as schizophrenia (Hennessy et al., 2004) and autism spectrum disorder (Hammond et al., 2008). Specific facial dysmorphology, resulting from prenatal exposure to alcohol, remains the key diagnostic feature of fetal alcohol syndrome (FAS) (Astley and Clarren, 2000; Hoyme et al., 2005).

Autism: One study with single photon emission computed tomography reported abnormally low regional cerebral blood flow (rCBF) in temporal and parietal regions of the left hemisphere in autistic children under anesthesia (Mountz et al., 1995). Similarly, Chiron and colleagues (1995) reported reduced resting rCBF in the left sensorimotor and auditory cortices and in Broca’s area in children with autism. While both circumstances led to a rightward shift in asymmetry during rest, there appeared to be a decrease in overall cerebral blood flow in children with autism (Chiron et al., 1999).

McKelvey et al. (1995) noted that in adolescent children with Asperger’s syndrome, right hemisphere abnormalities were present in temporal, frontal, and occipital lobes and in the cerebellum. Prior imaging reports in ASD have also identified Broca’s area as having abnormal structural asymmetry or language function (De Fosse et al., 2004; Herbert et al., 2002; Just et al., 2004). MRI scan volumetric analyses revealed a 27% larger right-side language-related area of the cortex (inferior lateral frontal and posterior superior temporal regions) in boys with autism compared to a 17% larger left-side area in controls (Herbert et al., 2002). A similar reversal of
the normal leftward asymmetry in language-related areas of cortex was reported in boys diagnosed with both autism and language disorder and in boys diagnosed with SLI, but neither in boys diagnosed neither only with autism who had normal language nor in boys with none of these disorders (DeFosse et al., 2004). These results suggested that reversed asymmetry in frontal language areas of the brain, with larger volumes on the right than on the left, may be differentially related to pediatric language disorders but not necessarily to autism. The role of serotonin has been identified as one possible mechanism for altered brain development in children with autism (Cook et al., 1997; Piven & Palmer, 1999).

ADHD: Reports of a smaller right-hemisphere frontal lobe in children with ADHD (Hynd et al., 1990; Castellanos et al., 1996) have been supported by evidence of reduced right-hemisphere dorsolateral prefrontal volume (Yeo et al., 2003). Investigators measuring gray and white volume in children with ADHD have reported reduced gray matter in both prefrontal cortices, especially on the right (Mostofsky et al., 2002) and in the right-hemisphere posterior cingulate gyrus, superior frontal gyrus, and putamen (Overmeyer et al., 2001). Reductions in white matter, however, were also noted for the left hemisphere in both of these studies. Sowell and colleagues (2003) reported evidence of increased gray matter density in the right occipital lobes of children with ADHD. These researchers compared distances between the center of the brain and the cortical surface and reported that brain surfaces of children with ADHD were reduced overall in the anterior temporal cortices and in the inferior dorsolateral prefrontal cortex, with reduced volumes noted on the right in the parietal cortex.

There are several reports of anatomical differences in the caudate nucleus in children with ADHD. Findings have indicated nearly every possible combination of symmetry and asymmetry in the caudate nucleus in children with ADHD, including reduced and symmetrical caudate nuclei, leftward asymmetrical caudate nuclei due to larger left-sided or smaller rightsided volume, and rightward asymmetrical caudate nuclei due to larger right-sided or smaller left-sided volume (Krain & Castellanos, 2006). Several studies have reported altered asymmetry of the basal ganglia due to a reversed right greater than left volume of the caudate nucleus, suggesting that deficient synaptic pruning during early development may have prevented the decrease in caudate volume that is seen in typically developing children (Castellanos et al., 2002). In addition to reports of abnormal asymmetry for the caudate nucleus in children with ADHD, there have also been reports of possible underdevelopment of the corpus callosum (Roessner et al., 2004).

Dyslexia: Research studies suggest that the left hemisphere is involved in the pathophysiology of dyslexia. Casanova et al. (2005) showed significant abnormalities in five left hemisphere structures involving the extrapyramidal and limbic systems: amygdala, hippocampus proper, parahippocampal gyrus, putamen, and globus pallidus. Analyses of postmortem specimens reported greater symmetry of the planum temporale in extrapyramidal and limbic systems: amygdala, hippocampus proper, parahippocampal gyrus, putamen, and globus pallidus. Analyses of postmortem specimens reported greater symmetry of the planum temporale in brains of dyslexic subjects, attributed to larger plana than normal on the right side of the brain (Galaburda, 1989; Galaburda et al., 1985). In addition, children with dyslexia showed significantly smaller right anterior lobes of the cerebellum (Eckert et al., 2003; Kibby et al., 2008).

Geschwind & Behan (1982) reported that lefthanders were more likely to suffer from various autoimmune disorders, and also were more likely to have manifested some form of developmental language disability. There is a differential mortality for left-handers and right-handers (Coren, 1994; Hugdahl et al., 1993). Coren & Helpen (1991) have suggested that left-handers are at greater risk for early death than are right-handers. They reported that left-handers die, on average, 7 years younger than do right-handers.

Hand preference and the performance of thumb-to-finger opposition by the right and left hands were tested in four samples: manic-depressives, schizophrenics, non-psychotic patients with diseases of the central nervous system and normal control subjects. The schizophrenics and manic-depressives both showed significantly more pure dominance (e.g. right-handed, and superior right thumb opposition) than the normal controls, while the non-psychotic patients with diseases of the central nervous system showed significantly more cross-dominance (e.g. right-handed, but superior left thumb opposition) than the normal control subjects (Metzig et al., 1975).

Benderlioglu and colleagues (2004) measured the symmetry of the participants’ fingers, palm heights, wrist diameters, elbow widths, ear sizes, foot breadths, and ankle circumferences. They found that, in general, the more asymmetry a subject exhibited, the more aggressive he or she would be. People with higher levels of asymmetry also have a harder time controlling their aggressive impulses.

Asymmetry of the mamillary body and fornix size was found in 37.1% (13/35) and 34.3% (12/35), respectively, of subjects with suggested hippocampal sclerosis. The prevalence of asymmetry of the thalamus, mamillary body and fornix was statistically significantly higher in the patients with mesial temporal sclerosis (MTS). Reporting MR imaging findings of asymmetric mamillary bodies and fornices can help in the detection, index of suspicion, and lateralization of MTS.

Schulter & Papousek (2008) investigated the possible relationship between established measures of body and brain asymmetries and individual differences in paranormal beliefs. Results indicated that a stronger belief in paranormal phenomena was associated with fluctuating asymmetry of finger length, and that this aspect of body asymmetry may be related to greater intraindividual variability in the degree of 'atypical' functional lateralization. This intraindividual variability index, in turn, significantly predicted strength of belief in the paranormal. Belief in the paranormal was also higher in women than men and it was negatively correlated with...
the education level. These findings suggest that a part of the variance of strength of belief in paranormal phenomena can be explained by patterns of functional hemispheric asymmetry that may be related to perturbations during fetal development.

Uitti et al. (2005) examined right vs left difference scores in a consecutive clinical series of 1,277 individuals diagnosed with Parkinson Disease. Asymmetric presentation of Parkinson disease features was a common occurrence in the clinical cohort. Multiple regression analyses showed that an increased discrepancy between right- and left-sided symptoms was significantly associated with a shorter disease duration, younger age at symptomatic onset, asymmetric initial symptom onset, hand dominance, and a positive self-reported family history of "other" neurodegenerative disorder. Hand dominance was related to the side of asymmetric disease such that left-handed individuals tended to have more severe disease on the left side of the body.

Asymmetry of body parts such as toes, popliteal crease levels, thumbs, cubital crease levels, and forehead and facial structures, are common in patients with localisation related epilepsy syndromes. It was concluded that body asymmetries in patients with seizure disorder is a useful clue to diagnosis of localisation related seizure and may provide clues for lateralising seizure origin in partial onset seizures (Fong et al., 2003).

Kaaro et al., (2008) found a significant asymmetry of the pineal gland in migraineurs compared with controls, and suggested that migraine's circadian component and its association with PFO may be linked to a lateralization defect during embryogenesis, which could be a result from abnormal serotonin regulation.

Kennedy et al. (1999), using anatomic and functional MRI techniques, analyzed asymmetries in the brains of three individuals with situs inversus totalis (SI). They found that the two major anatomic asymmetries of the cerebral hemispheres, the frontal and occipital petalia, were reversed in individuals with SI. Ihara et al. (2010), have shown that SI subjects had the same planum temporale (PT) asymmetry pattern as the controls, but a reversed petalia asymmetry pattern. The inferior frontal gyrus (IFG) asymmetry pattern varied within both groups, indicating a relationship between the rightward IFG and right-hemispheric language dominance. These results suggest that the developmental mechanisms underlying visceral organ asymmetries are related to that underlying petalia asymmetry but not to those underlying PT and IFG asymmetries, and that brain asymmetries might develop via multiple region-dependent mechanisms.

**Skeletal Asymmetries:**

The examination of the upper and lower limb asymmetries can be useful to medical scientists, archeologists, and anthropologists (Iscan & Shihai 1995; King et al., 1998), to the police and forensic experts and for medicolegal studies (Steyn & Iscan 1999; Mall et al. 2001). Significantly, this intra-individual variation in the size and shape of the left and sides of the body has been linked with low back pain (Friberg, 1983; All-Eisa et al., 2004). All-Eisa et al. (2004) showed that the higher the degree of asymmetry in the upper and lower limbs, the greater the likelihood of low back pain. Manning et al. (1998b) have shown that the ratio of the length of the 2nd and 4th digits (2D:4D) in right hands negatively predicts testosterone levels in men, and is negatively related to sperm number per ejaculate, sperm speed, and sperm migration. Men tended to have a lower 2D:4D ratio than women and in women 2D:4D was positively correlated with oestrogen and L.H. Determining the asymmetry of metatarsal bone development is essential to define whether the skeleton is developing correctly or pathologically.

Although subtle facial directional asymmetry is present in healthy individuals (DeLeon, 2007; Ercan et al., 2008; Schaefer et al., 2006), stronger directional asymmetry is often associated with conditions that disrupt normal craniofacial development, such as cleft lip and palate (Bock and Bowman, 2006), deformational plagiocephaly, or craniostenosis (Netherway et al., 2006). Changed patterns of directional asymmetry have been reported among individuals diagnosed with disorders in which facial changes may be a secondary consequence of abnormal brain development, such as schizophrenia (Hennessy et al., 2004) and autism spectrum disorder (Hammond et al., 2008). Specific facial dysmorphology, resulting from prenatal exposure to alcohol, remains the key diagnostic feature of fetal alcohol syndrome (FAS) (Astley and Clareen, 2000; Hoyne et al., 2005). Because craniofacial development of the face is intimately tied to the development of the brain, the question arises whether the increase of facial directional asymmetry associated with alcohol exposure correlates with a change in the asymmetry of the brain. Sowell et al. (2002) reported that individuals with severe prenatal alcohol exposure have reduced asymmetry of the cortical surface and gray matter density. Normal asymmetry is right-biased and particularly accentuated in the posterior inferior temporal lobes (Sowell et al., 2002).

An understanding of frontal sinus anatomy is important for clinical and forensic medicine. Frontal sinus radiographs could be a useful means of personal identifications (Harris et al., 1987a, b; Reichs 1993). A preoperative CT scans including the frontal sinus may be useful during a pterional craniotomy to minimize the inadvertent entry into the sinus in patients with a large amount of pneumatization (Patel et al., 2000).

**Vascular Asymmetries:**

The anatomical differences and vascular variations may be the cause of clots, aneurysms and a variety of other neurological problems (Osborn, 1999, Stehen, 1963). Quint et al., (1992) found severe intracranial
vascular abnormalities associated with absence or hypoplasia of the carotid canals and emphasized the importance of scrutinizing the skull base—even at routine screening CT examinations—for asymmetry of the carotid canals. Absence or underdevelopment of a carotid canal results from agenesis, apasia, or hypoplasia of the associated internal carotid artery (ICA) (Lie, 1968; Afifi et al., 1987; Quint et al., 1989). Such anomalies of an ICA have a high association with intracranial vascular abnormalities, specifically, aneurysm formation (Teal et al., 1973; Servo, 1977). Since the Carotid canals in the skull base form secondary to the presence of the embryonic ICA, asymmetry or absence of one (or both) of these canals suggest a congenital ICA abnormality and should prompt further evaluation to rule out the presence of potentially life-threatening intracranial vascular abnormalities, even in an asymptomatic patient. The ICA is specified by Bannister et al. (1999) to be a major source of the arterial supply to the cerebral hemispheres. Awareness about details and topographic anatomy of variations of the ICA may serve as a useful guide for both radiologists and vascular surgeons. It may help to prevent diagnostic errors, influence surgical tactics and interventional procedures and avoid complications during the head and neck surgery (Ovchinnikov, 2007).

The presence of a high common carotid artery (CCA) bifurcation should caution surgeons that the hypoglossal nerve lies in closer proximity and is more vulnerable (Lo et al., 2006). Carotid artery injury is one of the most feared, but fortunately least encountered complications during anterior cervical dissection (Lo et al., 2006). Low bifurcation of the common carotid artery may cause problems regarding anterior cervical dissection (Gulsen, 2009). Preoperatively documenting the level of the CCA bifurcation may be helpful in identifying those patients at increased risk of iatrogenic injury. The CCA bifurcation is of clinical importance due to its vascular access site for intravascular intervention. It has been preferred for balloon aortic valvuloplasty in children due to its advantages over femoral artery. Additionally it is also one of the commonest sites of atherosclerotic plaque formation (Fischer et al., 1990).

Unequal diameters of the vertebral arteries (VA) cause insufficiency in the vertebrobasilary circulation, which in turn results in vertebrobasilar ischemia (Kazui et al., 1989). It is reported that great differences in the diameter of the VAs at a level superior to the first cervical vertebra, play an important role in the etiology of the vertebrobasilar insufficiency (Kazui et al., 1989). The asymmetries reported in vertebral arteries become more significant if there is associated vertebral artery origin or proximal subclavian artery stenosis (Cloud & Markus, 2003).

Transarticular screws at the C1 to C2 level of the cervical spine provide rigid fixation, but there is a danger of injury to the vertebral artery. Madaw et al. (1997) concluded that variation in the morphology of C2 and an anomalous part of the vertebral artery associated with thinning of the lateral mass and pedicle may prevent adequate fixation by posterior placement of transarticular screws and expose the vertebral artery to risk of injury. High-resolution CT with three-dimensional reconstruction is mandatory before screw fixation is used to stabilise the C1 to C2 segment.

Naggara et al. (2008) demonstrated that intracranial ICA size asymmetry on 3D TOF MRA reached a sensitivity of at least 84% and a specificity of 88% to predict the presence of an underlying high-grade cervical ICA stenosis. In patients who undergo an intracranial MR angiography, ICA size asymmetry is an indirect sign of an underlying ≥70% cervical stenosis.

This sign could be used as a screening tool to detect severe cervical ICA stenosis on routine brain MR examination.

Bilateral simultaneous venous sampling of ACTH from the inferior petrosal sinus of patients with Cushings syndrome can distinguish adrenocorticotropin-secreting pituitary tumors (Cushing's disease) from other causes of the syndrome, principally ectopic adrenocorticotropin secretion from an occult tumor. It may also help in lateralization of the tumor (Mamelak et al., 1996). In the treatment of patients with Cushings disease, accurate preoperative lateralization of microadenoma is particularly important, because it can lead to successful selective adenomectomy of ACTH-secreting tumors by transsphenoidal microsurgery with preservation of normal pituitary function (Hayashi et al., 2008). Dopmann et al. (1999) concluded that the presence of a unilateral hypoplastic or plexiform inferior petrosal sinus can result in anomalous drainage from the pituitary gland that may lead to false-negative sampling results in patients with Cushing’s disease.

The femoral and radial arteries are often asymmetric. Ultrasound may be useful prior to arterial catheterization to identify the larger vessel (Eisen et al., 2006). The knowledge of variations in the anatomy of internal thoracic artery is important because of its recent use in the revascularization of the myocardium in patients with coronary artery disease. (Henriquez-Pino et al., 1993).

Knowledge of anatomic variability of the superior (STA), inferior (ITA), and lowest accessory (IMA) thyroid arteries may be helpful in certain clinical conditions. Therefore, anatomic arterial compatibility should be carefully evaluated in the preoperative stage of laryngeal transplantation maintaining in situ the donor's thyroid by terminal anastomoses between donor and recipient STAs. The lack of any individual thyroid artery might influence the distribution of autonomic supply that runs with thyroid vessels to the thyroid parenchyma. This appears functionally relevant in cases of traumatic or surgical lesions of the cervical sympathetic chain involving thyroid nerves. In fact, a restricted local autonomic control of thyroid activity might be related to
individual rami of thyroid nerves. The different frequencies of the presence of ITA and IMA in Caucasians and Asians should be taken into account during imaging or transcatheter ablation of inferior parathyroid adenomas, primarily the mediastinal ones. The feeding artery of these tumors, in fact, is frequently a branch of ITA (Eksen et al., 1975, Miller 1991) and their arterial supply can also be provided by an IMA (Krudy et al., 1980).

**Genital Asymmetries:**

Breast cancer is the most common malignancy among women. Asymmetrical breasts could prove to be reliable indicators of future breast disease and level of asymmetry can predict the degree of future risk and remedial process in advance. Asymmetry analysis is very important not only for identification of diseases but to predict future risk, cosmetic and reconstruction surgery (Bandyopadhyay & Maitra, 2010).

**Conclusion:**

Body asymmetries indicate the developmental instability of an individual (Watson & Thornhill 1994) and may indicate association with various disorders in the body. Knowledge and understanding of these asymmetries is important to achieve a good diagnosis and focus on an appropriate treatment and management plan. Because brain asymmetry develops prenatally, the recognition of asymmetry in neurodegeneration implies a possible relationship between the development of cerebral laterality and regional vulnerability in neurodegenerative diseases. This suggests that the study of cerebral asymmetry and laterality is likely to be relevant to a number of degenerative conditions that were previously considered to be only diseases of aging (Geschwind & Miller, 2001). Evidence from behavioral, electrophysiological, and functional neuroimaging studies should be used to understand how these developmental disorders differ so that accurate differential diagnoses and appropriate targeted techniques can be effectively applied for remediation. Likewise, there are various etiological factors: genetic, and environmental and functional, to be well understood for a proper diagnosis and thus appropriate to focus on a plan treatment.

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