Sex differences in cognitive abilities have been a widely discussed subject of interest already since the 1870s (for a review see [Shields, 1975](#shields1975)). Back then, research mainly utilised measures of head and brain size in an attempt to explain differences in cognitive capacities, as popularised by Gall’s phrenology (cf. [Cornel, 2014](#cornel2014); [Shields, 1975](#shields1975)). [more] In her 1975 review, Shields describes that many researchers at that time lacked the necessary impartiality to investigate the topic of sex differences, as they aimed “to discover the particular physiological determinants of female inadequacy” (p. 740). One example would be the research of [George Romanes (1887)](#romanes1887), who reported women to have smaller overall brain volumes, which he proposed to be directly responsible for their inferior intellect and increased emotionality ([Fee, 1979](#fee1979); [Shields, 1975](#shields1975)).

Other researchers pointed out that those presumed and described sex differences were inherently related to stereotypical gender roles ([Broverman et al., 1972](#broverman1972); [Sherman, 1967](#sherman1967); [Woolley, 1914](#woolley1914)). Even so, the view that the brains, as well as certain cognitive abilities of men and women are fundamentally different remained relatively common throughout both the minds of the vast population, as well as the scientific community. This theory is commonly referred to as the “gender differences hypothesis” ([Hyde, 2005](#hyde2005)).

With the advent of neuroimaging, new possibilities emerged for more objective research of sex differences in the cognitive neurosciences. Nevertheless, there still is no consensus on the exact neural mechanisms underlying those cognitive sex differences.

Several structural magnetic resonance imaging (MRI) studies and meta-analyses thereof found that the volume of the crania and brain lobes are generally larger in men than in women (Allen et al., 2003; Eliot et al., 2021; Goldstein et al., 2001), with some studies reporting a difference in total brain volume of up to 8-11% (Filipek et al., 1994; Goldstein et al., 2001; Swaab & Hofman, 1984). A study by Allen et al. (2002) found that while the gross volumes of brain lobes differs between the sexes, the proportional sizes of those regions to the total brain volume are nearly identical. Further, it has been reported that certain brain structures differ in (relative) size between the sexes. Some examples include larger volumes in the amygdala, putamen and globus pallidus in males, and larger volumes in the hippocampus and caudate in females (Cosgrove et al., 2007; Giedd et al., 1996a & 1996b). However, such findings are not uncontroversial, as sex differences in the volume of brain structures may disappear when correcting for total brain volume and/or intracranial volume (Choleris et al., 2018; Eliot et al., 2021; Tan et al., 2016).

Numerous studies also report that women have thicker cortices, as well as a higher grey-to-white matter ratio across cortical structures – even after correcting for the difference in total brain volume (Cosgrove et al., 2007; Sacher et al., 2013; Sowell et al., 2006). This effect was found to be especially robust in the inferior parietal and posterior temporal lobes (Sowell et al., 2006; Cosgrove et al., 2007). Generally, men were found to have a higher percentage of white matter (WM) and cerebrospinal fluid (Gur et al., 1999), whereas women were found to have 4-7% more grey matter (GM) than men (Eliot et al., 2021; Leonard et al., 2008; Ritchie et al., 2018). This difference is especially pronounced in the four lobes, the cingulate gyrus and insula (Allen, et al., 2003; Goldstein et al., 2001; Gur et al., 1999). Nevertheless, differences in grey-to-white matter ration have also been reported to disappear after correcting for total brain volume (Eliot et al., 2021; Leonard et al., 2008; Jäncke et al., 2014).

Some researchers consider sexual dimorphism to be stronger in the WM than in the grey matter (Allen et al., 2003; more). Even though men have a higher proportion of cortical WM, women have larger corpora callosa in proportion to their total WM volume (Allen et al., 2003; Gur et al., 1999; Dubb et al., 2003; Ingalhalikar et al., 2013).

Further, multiple studies have found that the corpora callosa of men and women differ in shape: Splenia are larger and more bulbous in women, whereas men have more tubular-shaped splenia, as well as larger genua (Allen et al., 1991; Dubb et al., 2003). Allen et al. (2003) proposed that WM tracts might be less sexually dimorphic than other WM components, such as glial cells and blood vessels.

Studies employing diffusion tensor imaging (DTI) investigated the architecture of WM and its fibre tracts found that over all age ranges, men tend to have increased measures of fractional anisotropy and decreased mean diffusivity than women. Higher measures of FA are thought to reflect increased axonal diameter, fibre bundle density and myelination, while the inverse relation holds for MD ([Boespflug et al., 2011](#boespflug2011); [Zasler & Kaplan, 2017](#zaslerkaplan2017)). However, in a similar vein to [Allen et al.’s (2003)](#allen2003) findings of women having larger corpora callosa in proportion to the rest of their WM, [Kanaan et al. (2012)](#kanaan2012) were able to show that the corpus callosum in women has higher FA than in men. This could be interpreted as women’s corpora callosa exhibiting greater efficiency.

DTI may not only be used to study isolated fibre tracts, but also to study the structural connectome of brain networks. Studies have found that women have a greater local brain network efficiency (Yan et al., 2011), as well as increased cortical connectivity (Gong et al., 2009) – independent of brain volume. A large-scale DTI study investigating sex-differences in the structural connectome by Ingalhalikar et al. (2013) found a higher proportion of intrahemispheric WM tracts in men and a higher ratio of interhemispheric connections, especially via the corpus callosum, in women.

[describe Hemispheric asymmetry]

Ingalhalikar (2013)

* Rather than investigating individual regions or tracts in isolation, the brain can be analyzed on the whole as a large and complex network known as the human connectome (Sporms, 2011). This connectome has the capability to provide fundamental insights into the organization and integration of brain networks (Bullmore & Sporms, 2009). Advances in fiber tractography with diffusion imaging can be used to understand complex interactions among brain regions and to compute a structural connectome (SC) (Hagmann et al., 2008). Similar functional connectomes (FCs) can be computed using modalities like functional MRI, magnetoencephalography, and EEG. Differences in FCs have revealed sex differences and sex-by-hemispheric interactions (Tomasi & Volkow, 2012a), with higher local functional connectivity in females than in males (Tomasi & Volkow, 2012b). Although SCs of genders have displayed small-world architecture with broad-scale characteristics (Iturria-Medina et al., 2007, Iturria-Medina et al., 2008), sex differences in network efficiency have been reported (Yan et al., 2011), with women having greater overall cortical connectivity (Gong et al., 2009). Insignificant differences between the genders were observed in a recent study on SCs of 439 subjects ranging in age from 12–30 y (Dennis et al., 2013).
* Using connection-wise regional and lobar analyses of DTI-based SCs of 949 healthy young individuals, we present a comprehensive study of developmental sex differences in brain connectivity
* Hausmann (2017)
  + Functional cerebral asymmetries (FCAs) refer to the relative differences between the left and the right hemispheres in some neural functions and cognitive processes and represent a relatively simple model for investigating functional connectivity in the brain. Although FCAs are a fundamental principle of brain organization (e.g., the vast majority of human individuals are left lateralized for language), about half of the variation in FCAs is attributable to individual differences (Kim et al., 1990). This variation was simply treated as random error, and was usually ignored in the past (Hellige, 1993).
  + In healthy adults, sex differences in FCAs have been reported for many cognitive domains, including language, spatial orientation, spatial attention, and face recognition. Although contrary findings, most studies reporting sex differences have revealed reduced FCAs in females compared with males (Voyer, 1996; Hausmann et al., 2003; Liu et al., 2009). Moreover, there is some evidence that women exhibit a greater degree of interindividual variability in FCAs, whereas FCAs in males are rather robust (Hausmann et al., 1998).
  + Merrill Hiscock and colleagues found stronger hemispheric asymmetry in males across a range of auditory (Hiscock et al., 1994), visual (Hiscock et al., 1995), tactile (Hiscock et al., 1999), and dual task interference (Hiscock et al., 2001) laterality tasks and concluded that, on the population level, sex differences in FCAs (i.e., larger FCAs in men than in women) are small but reliable (Hiscock et al., 2001). Daniel Voyer (1996, 2011) came to the same conclusion in his meta-analyses. Small effect sizes imply that only studies using a large sample will reliably find sex differences in FCAs.
  + Hirnstein et al. (2013) compiled behavioral data from 1,782 participants (885 females) and found that sex differences in the degree of language lateralization, as measured with a well-established verbal dichotic listening task (Hugdahl, 1995), were dependent on age, with the largest effect (Cohen’s d= 0.31) in adolescents. […] The sex difference in this task observed by Hirnstein et al. (2013) is in line with a recent study by Bless et al. (2015) that assessed language lateralization in over 4,000 participants with a smartphone application (iDichotic). This study also revealed greater language lateralization in men than in women, with a small effect of Cohen’s d = 0.18. Although effect sizes in sex differences of language lateralization are small, they are consistent with, for example, recent anatomical findings showing greater leftward asymmetry of the planum temporale (which overlaps with Wernicke’s area) in men than in women (e.g., Guadelupe et al., 2015), which is established very early in ontogenesis (Li et al., 2014).

[sex hormones may be the reason for differences in hemispheric asymmetry]

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  + Hellige (2001) suggested that differences occur because the hemispheric asymmetry is not the same for males and females. This is plausible in view of the evidence that sex hormones influence cognition and brain function both at critical stages of ontogenetic development (Geschwind & Galaburda, 1987) and in adulthood as various hormonal levels fluctuate over time (Kimura & Hampson, 1994).

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A popular theory proposes these differences to be rooted in differences in hemispheric asymmetry (e.g.: [Grabowska, 2016](#grabowska2016); [Ingalhalikar et al., 2013](#ingalhalikar2013); [Kovalev et al., 2003](#kovalev2003); see [Hirnstein et al., 2019](#hirnstein2019) for a review).

* Also Hirnstein et al., 2013
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According to this theory, male brains possess greater hemispheric asymmetry with more pronounced intrahemispheric connections, whereas female brains have stronger interhemispheric connectivity and thus, are organised more bilaterally. [where the left hemisphere would be clearly specialized for verbal processing and the right hemisphere for spatial processing. In females, the brain would be more “bilateral”, that is, both the left and the right hemisphere would be carrying out verbal processing]

[Ingalhalikar et al. (2013)](#ingalhalikar2013) interpreted those findings as male brains being structured in a way that facilitates spatial processing and coordinated motor action, while female brains promoting attention, memory and verbal abilities.

Eliot:

* s/g difference to be “massively reduced” (to roughly d =0.05) when covaried against TBV. Thus, larger brains have a higher proportion of WM than smaller brains, regardless of sex or even species (de Jong et al., 2017).

[Differences in GM/WM ratio]

* Cosgrove et al., 2013:
  + Allen et al. (2002) reported that the whole brain and most major subdivisions (e.g., hemispheres, frontal and temporal lobes, left parietal lobe, insula, and cerebellum) were significantly larger in men compared with women, but the proportional sizes of individual regions in relation to total hemisphere volume were similar. While men have greater brain volume (Gur et al., 1991), greater CSF volume or lateral ventricles (Gur et al., 1991; Grant et al., 1987; Agartz et al., 1992; Giedd et al., 1997), and greater sulcal volume (Gur et al., 1999) compared with women, ventricular volumes (Grant et al., 1987, Erdogan et al., 2004) and intracranial areas corrected for differences in cranial size do not vary between sexes (Agartz et al., 1992).
  + Gray and white matter volumes also vary by sex (Allen et al., 2003, Paus et al., 1996). When covaried for intracranial volume, height, and weight, women have a higher percentage of gray matter, whereas men have a higher percentage of white matter and CSF (Gur et al., 1999). The gray/white matter ratio was consistently higher in frontal, temporal, parietal, and occipital lobes; cingulate gyrus; and insula in women versus men (Peters et al., 1998; Gur et al., 1999; Allen et al., 2003; Goldstein et al., 2001; Haier et al., 2005).
* Allen et al., 2003: For all structures, male volumes were greater than female, but the gray/white (G/W) ratio was consistently higher across structures in women than men. Sexual dimorphism was greater for WM than GM: most of the G/W ratio sex differences can be attributed to variation in WM volume. The corpus callosum, although larger in men, is less sexually dimorphic than the WM as a whole. Several regions demonstrate pair-wise asymmetries in G/W ratio and WM volume. Both the cingulate gyrus and insula exhibit strong asymmetries. The left cingulate gyrus is significantly larger than the right, and the G/W ratio of the left insula is significantly greater than that of the right
* Ratio GM/WM
* WM se
* Cosgrove:
  + When covaried for intracranial volume, height, and weight, women have a higher percentage of gray matter, whereas men have a higher percentage of white matter and CSF (15). The gray/white matter ratio was consistently higher in frontal, temporal, parietal, and occipital lobes; cingulate gyrus; and insula in women versus men (9,15,17,19,20).
* Allen:
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* Goldstein:
  + However, regionally specific sex differences, relative to size of cerebrum, have been reported, and the direction of the sex differences differs depending on the brain region. These studies have reported, in women, relative to cerebrum size, greater cortical gray matter volume (Gur et al., 1999), larger volumes of regions associated with language functions [e.g. Broca’s area (Harasty et al., 1997) and superior temporal cortex, in particular planum temporale (Jacobs et al., 1993; Schlaepfer et al., 1995; Harasty et al., 1997)], and larger volumes of the hippocampus (Filipek et al., 1994; Giedd et al., 1996; Murphy et al., 1996), caudate (Filipek et al., 1994; Murphy et al., 1996), thalamic nuclei (Murphy et al., 1996), anterior cingulate gyrus (Paus et al., 1996), DLPFC (Schlaepfer et al., 1995), right IPL (Nopoulos et al., 2000), and white matter involved in interhemispheric connectivity (Allen & Gorski, 1987; Witelson, 1989; Highley et al., 1999; Nopoulos et al., 2000). Cell packing density, or number of neurons per unit volume, in the planum temporale was also greater in women than men (Witelson, 1995).
  + Compared to women, men have been found to have larger volumes, relative to cerebrum size, or differences in neuronal densities in other limbic and paralimbic regions [i.e. amygdala (Giedd et al., 1996), hypothalamus (Swaab & Fliers, 1985; Allen et al., 1989; Zhou et al., 1995) and paracingulate gyrus (Paus et al., 1996)], larger genu of the corpus callosum (Witelson, 1989) and overall WM volume (Passe et al., 1997; Gur et al., 1999), and greater CSF (lateral) ventricles (Agartz et al., 1992; Kaye et al., 1992) or sulcal volume (Gur et al., 1999)]. Some have argued that men have more neurons across the entire cortex (Pakkenberg & Gundersen, 1997; Rabinowcz et al., 1999). However, these findings are inconsistent with others (Witelson et al., 1995; Harasty, 1997), and suggest that sex differences in neuronal characteristics depend on the brain region and/or cortical layer assessed (Witelson et al., 1995).
* Eliot:
  + With the difference in overall brain size comes other male/female brain differences that are largely, if not exclusively, attributable to size rather than sex. One of these is GM/WM ratio, which averages 5.5 % larger in females across multiple studies. As brain size increases, there is a disproportionate increase in the denominator of this ratio, since larger brains need larger-caliber, more heavily myelinated axons to transmit action potentials across greater distances (Bush and Allman, 2003; Zhang and Sejnowski, 2000). Thus, the s/g difference in GM/WM ratio is largely eliminated when adjusted for total brain size (Leonard et al., 2008; Luders et al., 2002; Jäncke et al., 2015).
  + Furthermore, differences that are often portrayed as related to s/g (e.g., GM/WM ratio, or inter- vs. intrahemispheric connectivity ratio) are more accurately attributable to brain size, such that they distinguish large- from small-headed men (or large- from small-headed women) as well as they distinguish the average man from the average woman.

[more examples of differences]

* Numerous studies have reported that certain brain structures differ in (relative) size or shape differ between the sexes. Some examples include larger volumes in the amygdala, putamen and globus pallidus in males, and larger volumes in the hippocampus and caudate in females (Cosgrove et al., 2007; Giedd et al., 1996a & 1996b). Further, multiple studies have found that the corpora callosa of men and women differ in shape, especially in the splenium: Women have more bulbous splenia, whereas it is more tubular-shaped in men (Allen et al., 1991; more). However, such findings are not uncontroversial, as sex differences in the volume of brain structures may disappear when correcting for total brain or intracranial volume (Choleris et al., 2018; Eliot et al., 2021; Tan et al., 2016).
* Ingalhalikar et al., 2013:
  + Sex differences in the relative size and shape of specific brain structures have also been reported (Cosgrove et al., 2007), including the hippocampus, amygdala (Giedd et al., 1996 & 1997), and corpus callosum (CC) (Allen et al., 1991).
* Choleris et al, 2018:
  + Although a meta-analysis suggests that men have larger hippocampal volumes than women, this advantage disappears when hippocampal volume is adjusted for total brain or intracranial volume (Tan et al., 2016).

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