NEUROBIOLOGICAL AND EMPATHY DIFFERENCES BETWEEN GENDERS

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INTRODUCTION

The main difference between genders is the set of the sexual chromosomes, females are XX and males are XY. In the male Y chromosome there is the SRY gene, which initiates the sex differentiation. In the human development we found many processes group in two mechanisms: the first is organizational, and in this the SRY gene acts on bi-potential gonadal to differentiate it in testis. Then, with the formation of Sertoli and Leydig cells, these cells produce the anti-Müllerian hormone (AMH) and testosterone, these hormones act in the second mechanism, activational, promoting the defeminization and masculinization, respectively, of human fetus, producing different levels of gonadal sex hormones. The female development is the default program, which is activated in absence of SRY gene (Fig.1).

There are sex-dependent concentrations of sexual hormones receptors, as androgen receptor (AR) and estrogen receptor (ER), in different brain areas (Fig.2). These differences may be related with the differences in brain size between males and females.

The aims are see if there are neurobiological differences between genders, and if this influences the processing of the own and others emotions.

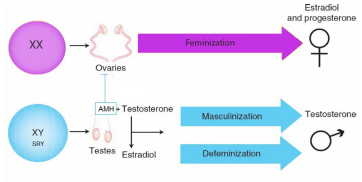

Fig.1 Organizational and activational mechanisms of sexual differentiation of human.

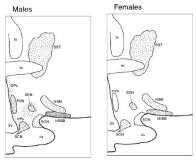

Fig.2. Schematic representation of the sex differences in the intensity of androgen receptor immunoreactivity (AR-ir) in the human hypothalamus. The dotted areas correspond to the median group intensity for AR-ir in males and females.

METHODOLOGY

Literature research on online databases (PubMed and ISI Web of Knowledge).
Literature research using the references of other articles previously read.

MORPHOLOGICAL AND NEUROCHEMISTRY OBSERVATIONS OF SEXUAL DIMORPHISM OF THE BRAIN

1. **The brain size:** The male brain is approximately 10% larger.
2. **The preoptic area:** It is subdivide in 4 nucleus: INAH-1 and INAH-3 are bigger and contain more cells.
3. **The suprachiasmatic nucleus:** There are more vasoactive intestinal polypeptide (VIP) only in young men.
4. **The bed nucleus of stria terminalis:** The central nucleus, BNSTc, is twice bigger and has more VIP and somatostatin (SOM) in males only in the adulthood (Fig.4). The BNSTc in women and male-to-female transsexuals are similar, whereas men and female-to-male transsexual have similar BNSTc. It is related with gender identity but isn't with sexual orientation (Fig.5).

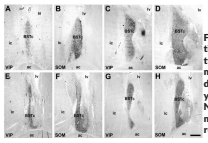

Fig.4. Representative photomicrographs depicting the BSTc in males (top row) and females (bottom row) in sections stained immunocytochemically for VIP (A, C, E, G) and SOM (B, D, F, G) during development. A, B, 14 years old; C, D, 39 years old; E, F, 16 years old; G, H, 32 years old. Note that the BSTc in males is larger than in females only in adulthood. Ac (Anterior commissure); ic (internal capsule) lv (lateral ventricle).

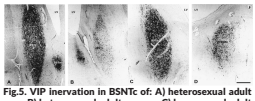

Fig.5. VIP inervation in BSNTc of: A) heterosexual adult man; B) heterosexual adult woman; C) homosexual adult man; D) transexual adult man. Note that (A) and (C) are similar, and (B) and (D) are similar too.

5. **The amygdala:** Kim et. al. (2012) divided it in three subregions: laterobasal (LB), superficial (SF) and centromedial (CM). The sexual differences have been found in the ratio of SF subregion, it is higher in males (Fig.6).

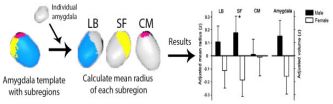

Fig.6. Process for each individual amygdala. The results indicated only significant differences (*) for SF subregions.

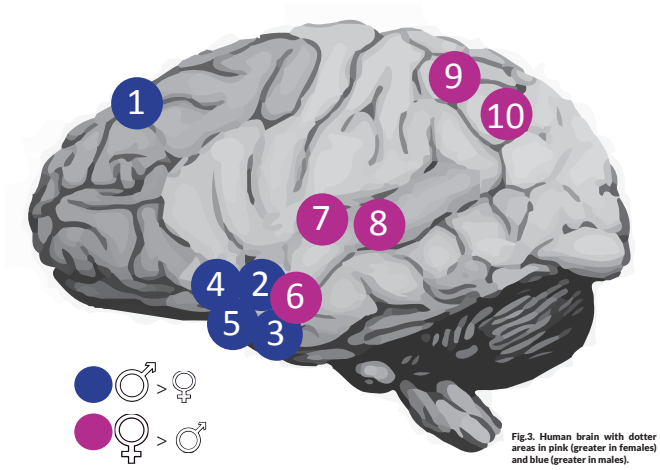

Fig.3. Human brain with dotter areas in pink (greater in females) and blue (greater in males).

6. **The ventromedial hypothalamic nucleus:** It has major metabolic activity in females.
7. **The hemisphere simmetry:** Males have right hemisphere larger than left one.
8. **The corpus callosum:** There is much controversy about the sexual dimorphism of corpus callosum, but the posterior region of it, the splenium, is bigger in women (Fig.7).
9. **The gray matter (GM) / white matter (WM) ratio:** The WM is lower than GM in females, and all together make greater GM/WM ratio in females than in males.
10. **The interhemisphere connectivity:** This is as a result of a greater number of fibers, in females reduces the functional laterality and it gives them an advantage to solve more complex situations due to the participation of two hemispheres. Males have got more intrahemisphere connections than interhemisphere, which is traduced to a functional laterality and tasks focused in one hemisphere or another (Fig.8).

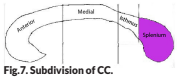

Fig.7. Subdivision of CC.

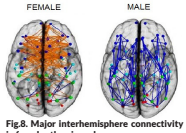

Fig.8. Major interhemisphere connectivity in females than in males.

EMPATHY

EMOTIONAL

Affective empathy involves the experience of a similar emotion of another person. It includes the human mirroring neuron system (hMNS).

Implicated areas: inferior parietal lobule (IPL), posterior superior temporal sulcus (pSTS), premotor cortex (PMC), and areas of lymbic system such as: amygdala, anterior insula (AI) and anterior cingulate cortex (ACC).

Modulates

Informs

Cognitive empathy involves the ability to know what another person is thinking or feeling and is similar to the concept of the "theory of mind".

Implicated areas: temporoparietal junction (TPJ), temporal pole (TP), posterior cingulate cortex (PCC) and medial prefrontal cortex (MPFC).

(Fig.9)

COGNITIVE

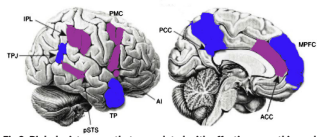

Fig.9. Pink depicts areas that are related with affective empathic, and green depicts areas that are related with cognitive empathy.

Amygdala, *the key structure*

Women activated more pronunciated the left amygdala than the right, which is more activated in males. This reflects different codificant strategies, left amygdala is related with conscient learning and right amygdala with unconscient learning (visual-espatial way).
There is higher amygdala activation in the first half of the menstrual cycle, due to the increment of the sex steroids.

Empathy of pain

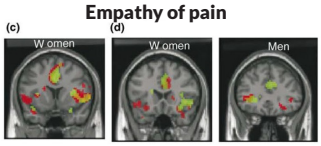

Fig.10. Overlapping brain activity in the AI and ACC when receiving painful stimulation oneself (green) or when empathizing with another person feeling pain (red), whereby (c) shows the activation of women perceiving cues indicative of their male partners feeling pain, (d) depicts the involvement of the same network when women (right) or men (left) observe an unknown but previously fair player receiving painful stimulation.

Regional gray matter volume

There are gender differences in regional gray matter volume (rGMV) in some areas, and this is in connection with major activation of these areas in males or females. In addition, there is relation between fetal testosterone and greater rGMV in men (Fig.11).

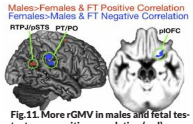

Fig.11. More rGMV in males and fetal testosterone positive correlation (red); more rGMV in females and FT negative correlation (blue).

CONCLUSIONS

- The SRY gene on the Y chromosome is responsible for testis determination in humans.
- The testis produce: AMH for inhibit the default feminine program, and testosterone for potentiate the masculine program.
- The sex differences of AR-ir in the various human hypothalamic areas may be the basis of sex differences in brain.
- The FT contributes to the organization of some GM structures in some sexually dimorphic way, but there are numerous factors likely contributes to sex differences in brain morphology.
- The sex difference in BSNTc volume only in adulthood suggests that marked sex-dependent organizational changes in brain structure are not limited to early development but may extend into adulthood.
- Males and females may use, at least in part, different strategies of cognitive and emotional processing which may contribute to gender differences in empathy.
- The functional MRI studies has also revealed: right amygdala activation males>females; left amygdala activation females>males.
- Women are more empathetic than men.

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Fig 1,9. Modification from: Christov-Moore et. al. Neuroscience and Biobehavioral Reviews, 2014. 46: 604-627; Fig 2. Fernández-Guasti et. al., 2000. Journal of comparative neurology, 2000. 425: 422-435; Fig 3,7. Patricia García Armenteros; Fig 4. Chung et. al. Journal of Neuroscience, 2002. Vol 22: 1027–1033; Fig 5. Swaab DF. Best Practice & Research Clinical Endocrinology & Metabolism, 2007. Vol 21: 431-444; Fig 6. Constructed with some images from: Kim et. al. NeuroImage, 2012. 60: 2054–2061; Fig 8. Ingalhalikara et. al. Proceeding of the National Academy of Science, 2014. Vol.2: 823-828; Fig 10. Vignemont and Singer. Trends in Cognitive Sciences, 2006. Vol.10 No.10.; Fig 11. Lombardo et. al. Journal of Neuroscience, 2012. 32: 674–680.