

The problem of the definition and quantification of reality

Marek Glezerman

Sackler School of Medicine, Tel Aviv University; Director, Research Center for Gender Medicine, Rabin Medical Center, Israel; President, International Society for Gender Medicine; President, Israel Society for Gender Medicine; Previous Chairman, Hospital for Women, Rabin Medical Center. — Received 16 April 2016.

Recently, a group of distinguished researchers from leading academic institutions in Europe and Israel published in the prominent scientific journal *PNAS* a study titled: *Sex beyond genitalia: The human brain mosaic*¹. The authors, led by Prof Daphna Yoel from Tel Aviv University, had set out to establish that the brains of male and females are not categorically different, that they are not dimorphic as is the categorical difference between the genital systems of the two genders. In order to confirm their hypothesis, the research team examined several large data sets of magnetic resonance imaging and of behavioral attitudes, comprising surveys which included thousands of men and women. The research focused on measuring brain voxels, which are volume values in a three dimensional space, and connectomas, which are a kind of wiring graph of connecting nerve cells. The overarching objective of the study was, to produce proof that brains of men and women resemble more a mosaic, comprised of specific overlapping functional regions, than distinct organs. The authors conclusion was that there is no such thing as distinct male and female brains. The conclusions of this paper have been disputed². The general and often cited dictum that “absence of an evidence is not evidence of absence...” applies also in this case. With the means deployed in their study, the authors did not find morphological differences between brains of men and women. An acceptable conclusion of this study might therefore have been that *with the tools* they applied, no morphological categorical differences between brains of men and women could be ascertained. Perhaps different tools, such as functional MRIs, might have yielded other results. Moreover, the MRI images which the researchers examined were comprised of “still images”, that is, images which by their very nature cannot represent and demonstrate dynamic functions of distinct parts of the brain. Looking at these images is more akin to examining a road map and draw conclusions about traffic patterns, without looking at the actual traffic. Finally, the paper makes no mention on whether MRIs from women and men were matched with any parameters, such as age, occupation, background diseases, hormonal status, time of the day etc. To find differences between two organs, organisms, entities and probably for most things in life, it is not enough to examine quantity and morphology, connections and voxels. Reality is not fully revealed from quantities or distributions of quantities. At the heart

of such evidence must be the *functionality* of the system. There are functional differences in various activity centers in the brain while performing physical or cognitive tasks or undergoing emotional experiences, but there are no morphological distinctions between brains, that experience happiness or sorrow, love or hate, empathy or compassion. Despite the substantial body of data on these issues, the subject research does not relate to this aspect and chose to exhibiting the absence of morphological differences between the brains of men and women. There was in fact no need for such an elaborate study that eventually corroborated a rather obvious fact that one cannot categorically arrive at a morphological distinction between a male and a female brain like one can concerning male and female genitalia. This adds but very little to scientific understanding of gender related research. Did any anatomists or pathologists ever claim that, in spite of known morphological differences in various brain nuclei and structures, they could determine the sex of a person by mere morphological and quantitative examination of their brain or even dissection of brains? Are slices of male brains supposed to be colored blue and those of women pink? The only areas where such distinctions can be made are relative to the genital systems and some distinct parts of the skeleton. It should therefore be obvious that whenever the terms “female brain” and “male brain” are used, the intention should be functional and not purely morphological, qualitative and not quantitative, statistical and not categorical. This is in fact true for most bodily systems and indeed, functionally, brains of women and men are different. Not better, not worse, neither stronger, nor weaker - just different.

Just consider the very brain cells, which of course differ chromosomally: The sex chromosomes of women comprise two XX chromosomes while those of men have an XY chromosomal pattern. Is it reasonable to assume that this fundamental cellular difference would be without consequences? The male brain is exposed to a completely different hormonal environment during intrauterine life than the female brain. Available overwhelming scientific data as to the crucial effect of testosterone on the developing male brain cannot seriously be challenged by morphometric imaging studies. The dimorphous development of the male and of the female brain is evident at the cellular level, the synaptic and dendritic organization, and also in the volume

of specific cell groups and nuclei³. In the human brain, dimorphic changes have been reported among others in the cortex, amygdala and in the hypothalamus. The latter governs central functions like reproduction, eating, and sleeping. Several language related tasks are more left lateralized in males, and more bilateralized in females, and women have apparently more brain speech centers than men⁴. In a study which involved one thousand young people it has been shown that the male brain has more connections *within* each hemisphere, while the female brain has more connections between the two hemispheres. That is, adjacent regions in the brain are more connected among men, while distant regions are more connected among women⁵.

The functional differences in the brains of men and women lead to a magnitude of somatic, functional and behavior differences. The effects of testosterone to which only the male fetus is exposed at a great magnitude prior to birth are numerous, including behavioral characteristics after birth, preferences for toys⁶, verbal skills, communication and many other features. Decreased testosterone levels, such as in times of acute or chronic stress in pregnant women due to war or during exposure to natural or personal disasters, have been associated with impaired neurodevelopmental outcomes, including attention deficit and hyperactivity in boys⁷. On the other hand, excessive prenatal exposure to testosterone has been implicated in the development of dyslexia and autism³. Ovaries and testes function differently, because of differences in hormone secretion by distinct brain regions (hypothalamus and pituitary). In the female brain, this secretion is pulsatile and that is the reason for the existence of the female menstrual cycle. In the male, the secretion is almost constant which is one of the reasons for the continuous process of sperm production. These brain regions look morphologically exactly the same, the hormones secreted are exactly the same – just the patterns of secretion in the brain of men and women are different, leading to fundamentally different functions of our gonads. Similarity in morphology but differences in function can be observed in virtually all bodily systems. Consider the human

heart: Except for size, the hearts in males and in females are indistinguishable from each other. Yet, more women than men who suffer from a heart attack will have open coronary arteries and atypical symptoms. Consider drugs: Prophylactic aspirin, taken by women will more often prevent strokes and if taken by men, will more often prevent a heart attack. Not always, just more often. Consider the gastrointestinal system: Passage time of food and drugs will more often be longer in women than in men, which has consequences for drug absorption and food digestion. More often, not always. And consider the brain: certain features, like spatial imagination, nest memory, multitasking capabilities, communicative strategies and many, many others may be more often present in one sex than in the other. More often, not always. In short, the definition of a male brain as opposed to a female brain should not be based on morphology but on functionality, or even better, on the relative prevalence of certain functional capabilities.

References

1. Joel D, Berman Z, Tavor I, et al. Sex beyond the genitalia: The human brain mosaic. *PNAS* 2015; 112: 15468-73.
2. Glezerman M. Yes, there is a female and a male brain: Morphology versus functionality. *PNAS* 2016 Mar 8. [Epub ahead of print] PMID: 26957594.
3. Baron-Cohen S, Lutchmaya S, Knickmeyer R. *Prenatal testosterone in mind*. London, England, Cambridge, MA: MIT Press, 2004.
4. Shaywitz BA, Shaywitz SE, Pugh KR, et al. Sex differences in the functional organization of the brain for language. *Nature* 1995; 373: 6515.
5. Ingahalikar M, Smith A, Parker D, et al. Sex differences in the structural connectome of the human brain. *PNAS* 2014; 111: 823.
6. Schulz KM, Molenda-Figueira HA, Sisk CL. Back to the future: The organizational-activational hypothesis adapted to puberty and adolescence. *Horm Behav* 2009; 55: 597-604.
7. Talge NM, Neal C, Glover V. Antenatal maternal stress and long-term effects on child neurodevelopment: how and why? *J Child Psychol Psychiatry* 2007; 48: 245-61.

Correspondence to:

Marek Glezerman

Research Center for Gender Medicine

Rabin Medical Center

Petah Tikva

39, Jabotinski Street

Israel

Tel +972-574-453600

email m@glezerman.com

www.isogem.com