Abstract

Brain sex does not always match the body sex, which is biologically acquired during intrauterine life and is affected by environmental factors that affect brain wiring developments of life events. The aim of present study was to investigate the neurocognitive functioning which is dependent on brain sex matters rather than the biological sex in normal healthy volunteers. A total of 126 participants were selected who filled and signed a special brain sex matter questionnaire as yes or no, which included a set of some special/specific and general questions. After, completing this questionnaire the participants were divided into four groups, group І: as very male brain sex, group ІІ: as very female brain sex, group ІІІ: as intermediate male brain sex and group ІV: as intermediate female brain sex respectively and then each group was subjected to a neurocognitive test by Leeds psychomotor battery tester. The psychomotor performance task and cortical arousal activity differences between very male brain sex and very female brain sex were found to be significant in total reaction time (TRT) \( p<0.01 \) but there was no significant differences in any other parameters \( p>0.05 \), While as, psychomotor performance task and cortical arousal activity differences between very female brain sex and intermediate female brain sex, significant differences were found only in movement reaction time (MRT) between the two groups \( p=0.005 \). Based on the finding it can be assumed that biological sex with very male brain sex matter has a superior neurocognitive function.

Keywords: brain sex, biological sex, neurocognitive function, psychomotor performance

Introduction

Brain sex does not always match the body sex which is biologically acquired during intrauterine life and is affected by various environmental factors (that affect brain wiring developments of life events) and sex hormones that act as neuromodulators on brain neurotransmitters therefore; brain sex is fashioned from these components which are energetic and interactive to constrain the gender behavior [1].

Previous studies have shown a biological dissimilarity between males and females were the influential tool of individual talent for how he or she think and react to others and these differences are based on brain sex rather than biological sex [2].

Additionally, human and animal research studies have revealed that males are mainly used as research subjects as their hormone levels do not differ episodically like in females, so any findings in male study individuals are interpreted to females, but; recently a psychoanalysis report of various gender neurocognitive studies show no
superior changeability than those with males, thus; brain gender differences are sexy [3].

Numerous, social cognitive studies have demonstrated that females of all ages are superior and outperform males on intellectual examinations necessitating emotion/recognition inter-relationships, additionally, empathy sex differences that appear with infancy period persist in development, thus brain sex be innately programmed and affected by culture, social learning and lifestyle than hormonal changes leads to more fixed experience that affect human brains [4].

Brain sex differences are not only functional, but many anatomical differences are documented through sophisticated radiological imaging and histochemical studies that revealed an area called ventral prefrontal cortex (VPC) which is responsible and involved for interpersonal judgment and social cognition and is larger in female than male. In addition the size of straight gyrus (SG) is more in female than male and influenced by prenatal hormones, where its size is correlated with social cognition and cognitive function regardless of gender [5].

Consequently, brain sex of biological gender can be assessed by gender questionnaire which could evaluate and estimate femininity versus masculinity apart from their biological gender depending on their personality and interest since; brain sex is correlated more with biological sex than with the brain anatomical changes [6].

Therefore, the aim of present study was to investigate the neurocognitive functions depending on brain sex matters rather than the biological sex in normal healthy volunteers.

**Subjects and Methods**

This study was carried out at Department of Clinical Pharmacology, College of Medicine, Al-Mustansiriya University, in Baghdad-Iraq from May to August 2015. Volunteers, were interviewed based on their health status. Exclusion criteria for the volunteers were psychiatric, sleep, neurological and other medical disorders. All volunteers were advised not to drink caffeine, stimulant drugs and alcohol containing beverage for at least five days before starting the study. The volunteers enrolled in this study signed a learned permission for their contribution to this study, according to the Declaration of Helsinki. The research protocol was endorsed and approved by an independent ethics and the scientific committee in Department of Clinical Pharmacology and College Medical Board.

A total number of 126 participants (60 males and 66 females) with mean age of 23 years (22-24 years range), were recruited from College of Medicine, Al-Mustansiriya University.

**Determination of brain sex**

All participants filled and signed a special brain sex matter questionnaire as yes or no, which included a set of special/specific and general questions and were scored ranging from 1-20. If YES was answered for 1, 3, 6, 7, 9, 10, 11, 14, 15, 17 the score was equal one point for each, while; if YES answered for 2, 4, 5, 8, 12, 13, 16, 18, 19, 20 the score was equal to zero point for each, after totaling the scores 1 score = very male brain sex, 20 scores = very female brain sex and between 1-20 scores = intermediate brain sex [7].

Then, use of calipers or ruler to measure digit length from middle of bottom creases to the top of the digit in cm, and measuring 2D:4D ratio which may be <1 (short ratio) or >1 (long ratio), also, this questionnaire correlates with index and ring digit lengths for both right and left hands (index finger shorter than ring finger indicates a male brain sex and vice versa). After, completing this questionnaire the participants were divided into four groups as very male brain sex group II: as very female brain sex, group III: as intermediate male brain sex and group IV: as intermediate female brain sex, then each group was subjected to a neurocognitive tests by employing a special device called as Leeds psychomotor battery tester (Zac-Gmbh.D-8346-Simbach/Inn), which measures following parameters:

**Cortical Arousal Activity (CAA)**

A preparation period of the test was permitted and supported, this test was performed in a dim room. The device calculates, records and lists the results. The Leeds psychomotor battery tester contains four red emitting diodes located in the corner of 1cm square in excess of a black panel, each participant should sit in front of device to ensure 75-100cm of distance between the device and eyes, which permits a binocular vision for flicker-fusion perception and discrimination, the flicker occurs at frequency that ranged from 1-60Hz. On an elevating trail, the participant observes the four red lights flickering and should press the key as soon as possible when as they emerge fused, this is called critical ascending or fusion frequency (ACFF), while; perception of fusion light till to be flickering called descending or flicker frequency (DCFF). The average of four-five fusions and flickers symbolizing and representing the cortical arousal activity, deterioration in either ACFF or DCFF indicating arousal disorders, moreover; when ACFF value more than 30 Hz (near 60 Hz) and DCFF value less than 30Hz (near 1Hz) indicating a good arousal activity, and from the above values a critical flicker fusion frequency (CFFF) can be estimated where CFFF= DCFF+ ACFF/2 [8].
Psychomotor Performance Task (PPT)

Leeds psychomotor performance device was applied for estimation of total reaction time in ms (TRT), which is regarded as an indicator for evaluation of sensory motor response to the critical stimuli. Participants placed the index finger on the central button and instructed to press urgent red appearance sites as soon as possible, the mean of five consecutive readings is recorded and listed on digital screen as total reaction time in ms (TRT) and recognition reaction time in ms (RRT). TRT represents the time for the onsets of a stimulus to the end of the reaction in ms, while RRT represents the time for the onsets of a stimulus to the beginning of motor action consequently, TRT minus RRT equal to movement reaction time (MRT) which represents the time from the end of stimulus recognition to the end of motor actions.

Statistical analysis

The results are presented as mean ± SE, and were analyzed by using paired and unpaired student t-test with a simple correlation, taking probability (p<0.05) as the lower border of significance.

Results

After, completing brain sex matter questionnaire, the participants were divided into four groups: Group I: 55 participants as very male brain sex (30 males and 25 females), Group II: 22 participants as very female brain sex (18 females and 4 males), Group III: 30 participants as intermediate male brain sex (20 males and 10 females) and Group IV: 19 participants as intermediate female brain sex (13 females and 6 males), figure (1).

Brain sex is correlated with short or long index finger of the dominant hand, in very male brain sex (VMBS) it is associated with short index finger as compared with ringer finger of the same hand while, in very female brain sex (VFBS) it is associated with long index finger as compared with ringer finger of the same hand figure (2).

Figure 1: Gender differences and participants in brain sex matters. VMBS( very male brain sex), VFBS( very female brain sex), IMBS( intermediate male brain sex), IFBS( intermediate female brain sex).

To establish the correlation and dependability between parameters of cortical arousal activity and psychomotor...
performance task among the enrolled participants, TRT is weakly correlated with RRT \( r=0.26 \) figure (3), while DCFF is highly correlated with ACFF \( r=0.79 \) figure (4).

**Figure 3:** Weak correlations between TRT and RRT \( r=0.26 \), in enrolled participants.

Moreover, there were no significant differences between very male brain sex and intermediate male brain sex regarding the psychomotor performance task and cortical arousal activity \( p>0.05 \), table (4).

**Table 4:** Psychomotor performance task and cortical arousal activity differences between very male brain sex and intermediate male brain sex.

<table>
<thead>
<tr>
<th>Neurocognitive variables</th>
<th>VFBS(n=55)</th>
<th>IMBS(n=22)</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>TRT ms</td>
<td>721.727±13.662</td>
<td>723.0±20.41</td>
<td>.330</td>
</tr>
<tr>
<td>RRT ms</td>
<td>397.18±9.343</td>
<td>373.38±7.98</td>
<td>.999</td>
</tr>
<tr>
<td>MRTms</td>
<td>324.58±0.018</td>
<td>349.56±0.062</td>
<td>.165</td>
</tr>
<tr>
<td>ACFF</td>
<td>31.31±2.2</td>
<td>31.59±0.25</td>
<td>.514</td>
</tr>
<tr>
<td>DCFF</td>
<td>28.14±0.19</td>
<td>28.11±0.23</td>
<td>.698</td>
</tr>
<tr>
<td>CFFF</td>
<td>29.61±0.04</td>
<td>29.64±0.043</td>
<td>.650</td>
</tr>
</tbody>
</table>

Data are expressed as mean ± SE, VFBS (very female brain sex), IMBS (intermediate male brain sex), TRT (total reaction time), RRT (reaction time), MRT (movement reaction time), ACFF (ascending critical fusion frequency), DCFF (descending critical flicker frequency), CFFF (critical flicker-fusion frequency). **\( p<0.01 \)**

In the same manner, there was no significant difference between intermediate female brain sex and intermediate male brain sex regarding the psychomotor performance task and cortical arousal activity \( p>0.05 \), table (5).
Table 5: Psychomotor performance task and cortical arousal activity differences between intermediate female brain sex and intermediate male brain sex.

<table>
<thead>
<tr>
<th>Neurocognitive variables</th>
<th>IFBS(n=30)</th>
<th>IMBS(n=18)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>TRT ms</td>
<td>738.53±11.351</td>
<td>723.0±20.41</td>
<td>.238</td>
</tr>
<tr>
<td>RRT ms</td>
<td>411.35±11.351</td>
<td>373.38±7.98</td>
<td>.456</td>
</tr>
<tr>
<td>MRTms</td>
<td>324.73±0.25</td>
<td>349.56±0.062</td>
<td>.892</td>
</tr>
<tr>
<td>ACFF</td>
<td>31.27±.23</td>
<td>31.59±.25</td>
<td>.551</td>
</tr>
<tr>
<td>DCFF</td>
<td>28.44±.16</td>
<td>28.11±.23</td>
<td>.648</td>
</tr>
<tr>
<td>CFFF</td>
<td>29.78±.03</td>
<td>29.64±.043</td>
<td>.390</td>
</tr>
</tbody>
</table>

Data are expressed as mean ± SE, IMBS (intermediate male brain sex), IFBS (intermediate female brain sex), TRT (total reaction time), RRT (recognition reaction time), MRT (movement reaction time), ACFF (ascending critical fusion frequency), DCFF (descending critical flicker frequency), CFFF (critical flicker-fusion frequency).

Results of the present study demonstrated a significant difference in both TRT and MRT mean differences in psychomotor performance task and cortical arousal activity between very male brain sex and very female brain sex. TRT differences were significant $p<0.05$, while MRT difference was highly significant $p<0.01$ (table 6).

Table 6: Mean differences in psychomotor performance task and cortical arousal activity between very male brain sex and very female brain sex.

<table>
<thead>
<tr>
<th>Neurocognitive variables</th>
<th>Paired Differences</th>
<th>95% CI</th>
<th>t</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>SE</td>
<td>Lower</td>
</tr>
<tr>
<td>TRT1-TRT2</td>
<td>7.63363</td>
<td>15.9498</td>
<td>3.39948</td>
<td>.56676</td>
</tr>
<tr>
<td>RRT1 - RRT2</td>
<td>1.04545</td>
<td>26.51590</td>
<td>5.65321</td>
<td>-12.80195</td>
</tr>
<tr>
<td>MRT1 - MRT2</td>
<td>8.66067</td>
<td>.07383</td>
<td>.01740</td>
<td>8.62395</td>
</tr>
<tr>
<td>ACFF1 - ACFF2</td>
<td>-.13636</td>
<td>1.58251</td>
<td>.33739</td>
<td>-.83801</td>
</tr>
<tr>
<td>DCFF1 - DCFF2</td>
<td>-.24091</td>
<td>1.78210</td>
<td>.37994</td>
<td>-1.03105</td>
</tr>
<tr>
<td>CFFF1 - CFFF2</td>
<td>-.05523</td>
<td>.21258</td>
<td>.04532</td>
<td>-.14948</td>
</tr>
</tbody>
</table>

1= very male brain sex, 2= very female brain sex, TRT (total reaction time), RRT (recognition reaction time), MRT (movement reaction time), ACFF (ascending critical fusion frequency), DCFF (descending critical flicker frequency), CFFF (critical flicker-fusion frequency). *$p<0.05$, **$p<0.01$

Discussion

The results of present study demonstrated that most of enrolled participants were very male sex brain matter (VMBS) while; the least fashioned as an intermediate female brain sex (IFBS), thus; this randomized and gender equalized study indicated that VMBS is predominant regardless of body gender types but, this brain sex matter classification was mainly corresponding with the numbers of enrolled male or female gender. These findings are parallel with other studies that showed females and males differ not only in their physical features or reproductive function, but as well in many other attributes, including the means they explain intellectual processes, this behavioral diversity is minimal and may be the consequences of experience developments and sex hormone effects on brain organization which lead to brain familiarity that was independent of physiological and biological predisposition [9].

Furthermore, this study showed a strong association with very male brain sex and short index finger of the dominant hand, while very female brain sex was associated with a long index finger of the dominant hand, whereas intermediate brain sex was mainly associated with equal index-ring length ratio. Many digit distribution ratios studies revealed that index finger (2nd digit) and ring digit (4th digit) is affected by prenatal androgen, thus, a ratio of 2D:4D if more than 1 indicates a long index while if the ratio less than 1 indicates a short index digit, the difference in ratio of 2D:4D is sexually dimorphic more in males than females [10]. A numeral of studies has shown a correlation of 2D:4D ratios between behavioral types regarding brain sex, thus; estradiol: testosterone ratio is correlated with 2D:4D ratio, moreover, female with congenital adrenal hyperplasia has higher 2D:4D.
ratio, while male with a testicular feminizing syndrome (androgen insensitivity syndrome) is associated with lower 2D:4D (female style) [11].

Short 2D:4D ratio was associated with good academic performances and psychomotor performances in male and lesbian attitude in females, while the long 2D:4D ratio was associated with good tactile perception and high intelligent scores in male, but with personality disorder in females [12].

Furthermore, this study pointed out to the significant neurocognitive differences among brain sex matters. Very male brain sex fashionable better reaction time than very female brain sex as showed with shorter total reaction time as compared with long total reaction time in very female brain sex, while intermediate female brain sex to react better than very female brain sex at movement reaction time. They differed significantly, therefore, very male brain sex had better psychomotor performance and arousal activity in comparison with other brain sex matters.

Female and male brains have significant differences, male brains use left hemisphere for language function and right hemisphere for visuo-spatial stimuli processing, while female brains use right and left hemispheres for language and visuo-spatial stimuli processing. This makes male brains more task oriented and more systemizing than female brains and less affected by emotional stimuli [13].

Animal models studies have shown that, if a rodent male at post delivery period is deprived of androgen by castration, a female behavior will be expressed, while if a rodent female is exposed to androgen a male behavior will develop; these effects explain the hormonal effect on brain behaviors at postnatal life which is not true to later life, therefore, optimal androgen level may be responsible for brain sex behavior since a low level in male and high level in female improved psychomotor performances thus explaining the psychomotor performance changes throughout menstrual cycle [14].

Gender individuality and brain sex orientation are related to the size of hypothalamus which is larger in male than female [15], this clarified the domination of very male brain sex matter in most of the participant males in the current study; furthermore, corpus callosum is larger in female, permits more communication between right and left hemispheres in females, frontal lobe which is a site for problem solving and decision making also is larger in female, but parietal lobe which is a site for sensory processing and space perception is larger in male. This suggests a different gender pathway in stimuli processing and reaction [16], also female brains have more serotonin receptors with low serotonin transporters than male [17], this explains the low female response to the cortical arousal and psychomotor stimuli in the present study.

Moreover, male outperform female in the most spatial and psychomotor tasks, but in contrast female outperform male in verbal memory consequently, brain function and structure changes are more correlated with biological sex but, preference of gender trait for feminine or masculine styles is certainly created by brain sex matter depending on nature and nurture [18].

Finally, male brains are wired from front to back with a few inter-sphere connections and vice versa in the female leads to high-quality sensory motor speed accuracy in male and good face-social cognition in female [19].

**Conclusion**

Taken together the results of present study demonstrated that most of enrolled participants were very male sex brain matter (VMBS) while; the least fashioned as an intermediate female brain sex (IFBS) and biological sex with very male brain sex matter has superior neurocognitive function.

**Acknowledgments**

The authors would like to thank the staff of the College of Medicine, Al-Mustansiriya University for their great cooperation during this entire study.

**Conflict of interest**

None declared.

**References**


