Gender related peculiarities of amygdala deactivation during movements

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Aims and objectives

Unlike sexual characteristics, which are the physical qualities that separate the two sexes of an organism, the neurological differences are not visually apparent and therefore hard to study. Psychological sex differences are thought to reflect the influence of genes, hormones and social learning interaction on brain development throughout the lifespan. More and more evidences arise showing the gender related human brain differences in terms of functional organization [1] and even brain volume [2], although ‘gyrification’ index, doesn't differ significantly between genders [3]. Some differences are subtle, but just some of them appear to be more prominent. Sex differences in human behavior show adaptive complementarity: males have better motor and spatial abilities, whereas females have superior memory and social cognition skills [4]. In all supratentorial regions, males had greater within-hemispheric connectivity, whereas between-hemispheric connectivity predominated in females. This effect was reversed in the cerebellar connections [4].

Handedness associated anatomical brain asymmetry was found in males, but not in females, suggesting sex differences in the cortical organization of hand movements. Right-handed males showed a significantly deeper central sulcus on the left hemisphere than on the right, while no interhemispheric asymmetry was found in females [3]. Some of the brain diseases demonstrate distinct gender-related specificity and prevalence, e.g. multiple sclerosis, Alzheimer’s disease - two times often occur in females than in males, and on the other hand, autism, Parkinson’s occurs more often in males [2, 5]. However, this field of research has spurred an equally long history of debate as to whether inherent differences in the brains of males and females predispose the sexes to stereotypical behaviors, or whether such claims reinforce and legitimate traditional gender stereotypes and roles in ways that are not scientifically justified - so-called neurosexism [6].

Functional MRI is often used in fundamental and clinical studies. Because of its robust physiologic basis and good spatial resolution to date fMRI is widely used for brain mapping in thousands of clinical and scientific departments all over the world, and accepted as the standard clinical procedure for brain mapping in the USA as the neurosurgical preoperative approach. Brain mapping of motor regions in the cortex appears to be one of the oldest and most widespread fMRI technique in clinical practice. Nevertheless the presence of huge amount of studies utilizing this task for brain mapping - gender differences in patterns of brain activation under motor task execution seem to be underinvestigated. We propose fMRI analysis of the brain activated by a movement task for estimation of gender specific motor brain network peculiarities.
Methods and materials

Twelve healthy subjects (6M, 6F, 20-39 years old) were studied by fMRI with 1.5T SIGNA EXCITE (GE). FMRI data were obtained using GE EPI pulse sequence with following parameters: TR/TE=3000/73 ms, voxel size=4x4x6 mm. The task paradigm lasted 3 minutes and consisted of three blocks of simple finger tapping task separated with rest periods, each started with the voice command. The brain maps with the regions of activation were built with GLM model. Model based ICA analyses was done using GLM design matrix (software package FSL5.0).
Results

From the analysis of the brain maps gender differences in total brain activation were found. In males the volume of activation was much smaller (17.6 cm$^3$) in comparison to females (53.1 cm$^3$). Also, we have found high linear correlation of the general volume of activation and maximum task-related BOLD signal change in masculine and feminine subpopulations Fig. 1 on page 6. Common regions of activation in contralateral primary sensory-motor cortex, supplementary motor area, and ipsilateral cerebellum were found. Also, we have found out additional activation of bilateral ventral premotor cortex, bilateral frontal cortex and contralateral hemisphere of the cerebellum in females Fig. 2 on page 6.

Data suggesting that the pattern of brain fMRI activation differs in male and female subjects were shown. Our results showed that females need more neural substrates for motor control and some cognitive support and enlarged brain activation, while the men use less cognitive control of movement execution. To date, metabolic [7] and structural [3] sex related Rolandic area differences were shown. Greater gray matter thickness and N-acetyl export concentration in the primary sensorimotor cortex were shown in females [7, 8]. Interhemispheric asymmetry in the depth of the central sulcus region that controls arm movement is present in male subjects, this asymmetry was not found in females [3]. In addition, there is evidence that sex hormones influence anatomical characteristics of the primary motor cortex. For example, gonadectomy in male rats decreased the span of horizontal neuronal connections within the primary motor cortex, whereas this decrease was significantly lessened in animals that received exogenous testosterone [9].

Common regions of deactivation were found for male and female subgroups. They accounted regions of the default mode network - precuneus, posterior cingulate, medial prefrontal and parietal cortex Fig. 3 on page 7. Selective deactivation of the ipsilateral primary sensory-motor area and left amygdala (-26, -16, -18, MNI152) was found in males Fig. 3 on page 7 Fig. 4 on page 8.

The amygdala has structural differences in males and females, including size and sex hormone receptors [10]. Left and right amygdalae are important key nodes in a neural network that process emotional stimuli. It is hypothesised that the amygdala plays an important role during the encoding and generation of responses to negative and positive stimuli [3]. It is believed that women are more emotional than men. In a stressful environment men may expend less effort when using the cognitive regulation of the negative emotions, due to greater use of automatic emotion regulation. On the other hand, women may use positive emotions for the reappraising negative emotions to a greater degree. [3]. Women may be offsetting their negative affect with an increase in positive affect, and hence show no change in amygdala responses, but an overall decrease in negative affect as indexed by self-report. However, men showed greater decreases in amygdala activity during emotion regulation, along with lesser control-
related prefrontal activity during cognitive regulation. [3]. In a study of pain perception it has been proposed that the observed deactivations of the amygdala indicate a cognitive strategy to adapt to a distressful painful event. Altered activity in the amygdala may be part of a mechanism to attenuate pain-related stress responses [11]. In our study, left amygdala deactivation in men supposes specific emotional suppression during the movement execution in unpleasant enclosed restricted space, while in women we haven't figured out robust deactivation of the amygdala, on the contrary they had additional regions of activation in the frontal cortex. Thus, we can speculate, that MRI scanner environment or constant increased attentional demand during the fMRI scan can evoke additional emotional response in different genders in a different way and as a result change the pattern of brain activation.
**Fig. 1:** Total volume of brain activation in males (blue) and females (red). Correlation of the total volume of activation and maximum task-related BOLD signal change.

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Fig. 2: Topography of brain activation in males (blue) and females (pink) during the hand movement.

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**Fig. 3:** Topography of brain deactivation in males (green) and females (red) during the hand movement. Left amygdala, ipsilateral sensorymotor cortex and default mode network regions deactivation was found in males. Default mode network deactivation was found in females.

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Fig. 4: Left amygdala deactivation in males during the movements.

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Conclusion

Our results suppose new evidence for gender related differences in the functional brain organization. Results also give us background for further subdivision of the fMRI normative basis from which we investigate functional brain changes in patient population.
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