Age-related peculiarities of the default mode (DMN) and sensorimotor (SMN) brain network interaction: fMRI study

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**Aims and objectives**

The process of normal brain development across the lifespan comprises gradual changes in its structure and functionality. Task-performance and cognitive improvements in childhood and motor and cognitive decline in elderly are underlied by these changes. However, ageing brain compensatory processes may allow sufficient maintenance of the motor performance level in some individuals. In the early childhood, at the period of intensive myelination and synapse quantity growth, analysis of these changes allow to evaluate the level of brain maturation, and in the elderly - level of degeneration. The brain is organized into a large number of interconnected neural networks. These networks are highly dynamic and have the capacity for adaptation. Neural plasticity can be defined as any observable changes in neuron structure or function and is the neurological mechanism by which the central nervous system encodes novel behavior [1]. Most of the modern studies of the age-related brain changes evaluate regional peculiarities of the structural, metabolic and functional characteristics. Thus, evaluation of the brain network interaction across the lifespan gives us a new approach to the age-related neural plasticity investigation.

The movement execution is supported by the increased activity of the sensory-motor neural network (SMN) (primary motor cortex, BA4; primary sensory cortex, BA3; secondary and supplementary motor area BA6; cerebellum, extra- and pyramidal motor pathways) [2]. Also impellent act is accompanied by the cortex deactivation [3]. Brain regions of the precuneus, dorsal cingulate cortex, medial temporal, lateral parietal and medial prefrontal cortex were shown to be functionally connected, and are deactivated during different tasks execution [4]. It was assumed that they form so-called ‘default mode network’ (DMN) because of its specific functioning in the resting-state at the time of mind-wandering, memory recall, or future planning, without any external input [5]. Also this network was shown to decrease the activity specifically to the task execution. More and more evidence appear about the DMN functional connectivity disruption in the brain neuroplasticity failure, like Alzheimer disease, schizophrenia, dementia, depression [5].

Considering the peculiarities of the brain age-related functional connectivity, we propose analysis of the SMN and DMN interaction during the hand movement in different age groups for the fMRI pattern of the brain maturing and ageing visualization and evaluation.
Methods and materials

Cohort of 29 volunteers (13#, 16F, 7-86 y.o.) with no signs of neurological disorders was examined with fMRI. Subjects were divided into three groups considering the age. Group 1 accounted 8 volunteers (3#, 5F, 7-16 y.o.). Group 2 accounted 16 volunteers (6#, 6F, 24-48 y.o.). Group 3 accounted 9 volunteers (4#, 5F, 51-86 y.o.). All subjects were right-handed and gave informed consent about participation in the study, approved by local bioethical committee. During the scan volunteers were asked to lay motionless, except executing right hand finger tapping task, with closed eyes and supine palms, thinking of nothing in particular Fig. 1 on page 4.

Full-brain fMRI data were acquired using MRI scanner 1.5T Signa ExciteHD (General Electric, USA). Multislice T2*-weighted gradient echo EPI images were obtained with such parameters: TR/TE=3000/71 ms, FA=90°, NEX=1, voxel dimensions 4x4x6 mm. 25 slices covering brain from the cerebellum to the vertex for each volunteer were acquired. High resolution T1-weighted anatomical scans were obtained for each subject with pulse sequence FSPGR. Parameters for pulse sequence TR=11.6 ms, TE=5.2, TI=450 ms, voxel dimensions=0.98x1x1.5 mm. Model based fMRI data were acquired during 4 min scanning session, 50 timepoint images were received. Task execution was formed into 3 blocks of rest and activation, each lasting for 30 s, so the period of paradigm oscillation was 60 s Fig. 1 on page 4. Thus the frequency of modelled oscillation was $f=0.0167$Hz.

Model based fMRI data processing was carried out using FEAT, part of FSL (FMRIB’s Software Library) [6]. Activation and deactivation were modelled with GLM as an opposite contrasts. Model based two-step ICA analyses was done using GLM design matrix. Single subject and group ICA analysis was carried out using MELODIC, part of FSL [7].
Images for this section:

![Diagram of finger tapping paradigm scheme](image)

**Fig. 1:** Simple finger tapping paradigm scheme.

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Results

RESULTS
Using the GLM and ICA methods for fMRI data analysis we have identified regions of activation, deactivation and functional connectivity as an extrapolation of the engaged neural networks interaction during the finger movement in different age groups.

Brain activation topography

Activation

GLM analysis of the fMRI data revealed peculiarities of brain activation during the right hand motor task execution for Group 1, 2 and 3. Common regions of activation were found in the contralateral (left) brain hemisphere, particularly in the primary sensorimotor cortex (M1/S1_con), supplementary motor, ventral and dorsal premotor areas (SMA_con, PMV_con, PMD_con), and insula (Ins_con) Fig. 2 on page 10. Ipsilateral brain hemisphere activation was found in the ventral premotor cortex (PMV_ips) and cerebellum (Cereb_ips). Each group had some specific sites of brain activation. Additional regions of the contralateral brain hemisphere activation were found in the Group 1 and 2. Particularly, Group 1 - putamen, Group 2 - middle frontal gyrus. Group 3 additional activation in the contralateral brain hemisphere was found in the regions of thalamus, pyramidal tract, inferior part of middle and inferior temporal gyri and adherent occipital cortex. Also Group 3 activation of the ipsilateral hemisphere was seen. Particularly, dorsal regions of superior and middle frontal gyri, regions of middle thalamus, inferior regions of precentral gyrus, insula, regions of middle lateral parietal cortex, angular gyrus, superior temporal gyrus. Volumes of activation for three groups (V1_act, V2_act, V3_act, #m^3) were (51.9, 102.5, 125.3) Fig. 4 on page 10.

Deactivation

Only subjects from the Group 2 presented a well-known pattern of brain deactivation described as DMN: precuneus (pC), posterior cingulate cortex (PCC), medial prefrontal (MPFC), right and left inferior parietal cortex (RIPL and LIPL, respectively) and ipsilateral primary sensorimotor cortex (M1/S1_ips) (Fig. 3A) Fig. 3 on page 10. Also, some subjects from Group 2 revealed deactivation of the superior frontal gyrus bilaterally, hippocampus bilaterally, rostral part of the middle temporal gyrus and inferior part of the central sulcus. The pattern of deactivation significantly differs in the Group 1 and 3. Only some of the subjects from the Group 1 revealed M1/S1_ips deactivation. Group 3 volunteers revealed pC and PCC deactivation (Fig. 3B) Fig. 3 on page 10. Volumes
of deactivation for three groups ($V_{1\text{deac}}$, $V_{2\text{deac}}$, $V_{3\text{deac}}$, #m$^3$) were (6.3, 125.6, 4.4) Fig. 4 on page 10.

Ratios of brain activation/deactivation ($V_{\text{rat}1}$, $V_{\text{rat}2}$, $V_{\text{rat}3}$) were (8.2, 0.8, 28.5). Thus the activation-deactivation balance is only shown for the adult age (Group2). The process of activation prevailed in the juvenile and elder groups.

**BOLD signal change**

We haven't found any age-specific changes of the BOLD signal amplitude in the regions of activation, so #A$_{\text{act}}$#1.1±0.4% (using threshold Z#2.3), but we have found progressive BOLD signal amplitude increase with age in the regions of deactivation for the Groups 1, 2, 3: #A$_{\text{deact}}$#(0.76, 1.03, 1.56)% respectively.

**Functional connectivity**

**SMN**

The results of ICA analysis revealed several neural networks to be functionally connected during the movement execution. For all three groups functional connectivity was found in the region of SMN ($M1/S1_{\text{con}}$, $SMA_{\text{con}}$, $Cbell_{\text{ips}}$) which supported the results of GLM analysis. In Group 3 region of $M1/S1_{\text{ips}}$ was also functionally connected with SMN. Frequency spectrum had two main frequencies $\nu1=0.0153±0.0051\text{Hz}$ and $\nu2=0.0204±0.0051\text{Hz}$. These frequencies reside (considering the measurement accuracy) in the range of the main frequency of the paradigm - $f$. BOLD signal oscillation correlated with the paradigm of activation ($P<0.000$), thus this functionally connected neural network directly correlated with the movement execution.

**DMN**

Also functional connectivity was found in the earlier described regions of DMN for the Group 2 and 3. But ICA analysis revealed two different independent components with the different frequency profiles, which topographically were specific to the regions of the DMN. First component had a high correlation coefficient with the deactivation ($P<0.000$), thus revealing task-induced deactivated DMN$_{\text{deact}}$, and the second one had a low correlation coefficient to the paradigm execution ($P<0.420$), and might be the sign of DMN functioning independently of deactivation (DMN$_{\text{ind}}$). Frequency spectrums of the DMN$_{\text{ind}}$ and DMN$_{\text{deact}}$ were different also, but varied among the studied cases.

**Visual cortex**
For all three groups functional connectivity in the regions of the cuneus and the lingual gyrus bilaterally was found with high correlation with the paradigm (P<0.000). Frequency spectrum has two peak frequencies $v_1=0.0204\pm0.0051$Hz and $v_2=0.0357\pm0.0051$Hz.

**Fronto-parietal network**

We have found out functional connectivity in the regions of frontal and parietal cortex, angular/intraparietal, anterior part of middle frontal, and the dorsal part of inferior frontal gyri bilaterally for the Group 1 and 2. Described regions are well known to form fronto-parietal 'grasping' neural network, FPN. The FPN functioning was shown to have a high level of correlation with the paradigm (P<0.01), the frequency spectrums of BOLD oscillations were comparable, but a little bit different for Group 1 and 2 (Group 1: $v_1=0.0204\pm0.0051$Hz and $v_2=0.0408\pm0.0051$Hz; Group 2: $v_1=0.0153\pm0.0051$Hz and $v_2=0.0357\pm0.0051$Hz).

**DISCUSSION**

The human brain tends to change all the life long. Plasticity of neural networks across the lifespan and the boundaries of the changes remains one of the hottest subject of the research. Age, sex, stage of the development, motor learning-relearning, pathological processes are only a few factors that cause changes in the brain. We tried to find age-related peculiarities of the fMRI patterns and neural networks interplay during the simple movement execution to elucidate the basis for the evaluation of the normal and pathological fMRI data in different age groups.

It is wide known that cortical control of the simple unilateral movement is supported by the neural network: M1/S1$\text{con}$, SMA$\text{con}$, PMV$\text{con}$, PMD$\text{con}$, Cbell$\text{ips}$ [1, 2, 8, 9]. Neural coding of the particular learned movement, as a scheme of the limb movement in the space, is formed in the PMV, and is independent from the target limb, used for the execution of the impellent act [8]. Possibly, further process of limb lateralization takes place in the PMD$\text{con}$ and SMA$\text{con}$. Then through the efferent fibers signal follows to the Cbell$\text{ips}$, where the process of movement initialization arises, and in the lateral parts of the cerebellum muscle coordination take place. From the Cbell$\text{ips}$ and through the ventrolateral thalamus signal arrives to the somatotopically organized M1/S1$\text{con}$, where the efferent neural signal follows to the alfa-motoneurons of the anterior horns of the spinal cord, controlling muscle contractions [8].

We have found out age-dependent increase of the volume of activation. Enlargement of activation in older subjects was demonstrated earlier, but notably in those cases where the level of movement execution and accuracy remained unchanged [10]. Increase of the extent of activation means compensatory mechanism need to maintain the movement accuracy. Decline in muscle mass and strength is seen in older human and animals [11], and also lost of anterior horn cells was shown [12], which might impair the transformation
of the descending corticospinal impulses into the generation of force, and lead to an increased effort in maintaining task performance [10]. Also it was shown that unilateral hand movement causes as lateralized brain activation (M1/S1 <sub>cor</sub>, Cbell<sub>ips</sub>), but also bilateral SMA, PMV, PMD, Ins [10]. Activation of the 'grasping' fronto-parietal network (intraparietal sulcus and frontal regions) also was shown [10].

As in our study, enlargement of the clusters of activation of the ipsi- and contralateral hemispheres (superior frontal gyrus, frontal operculum, insula and intraparietal sulcus), and cerebellum was shown earlier [1, 10]. Younger subjects were shown to be more susceptible to the deactivation of M1<sub>ips</sub> during the hand grip. Also there were no correlation of the BOLD signal change and the age of the subject. No gender differences in activation pattern were found also.

It was shown earlier [10] that activation of PMv (BA 44) and parietal regions (intraparietal sulcus/supramarginal gyrus) during the hand grip support the idea of grasping circuit functioning during the described movement and that it might be the ubiquitous part of fMRI pattern activation, that is suggested of continued monitoring of hand performance, rather than particular type of hand task itself.

M1<sub>ips</sub> activation could be seen in older population, particularly due to the need of additional control of hand contraction. While the additional recruitment of brain regions is observed during the hand motor task performance, deactivation of M1<sub>ips</sub> is often seen in the younger and adult populations, but not in the older one [2, 10]. It might be due to the reduced intracortical inhibition in motor cortex of the older subjects [13]. The premotor regions activated increasingly in older subjects are located even more anterior to the PMD, pre-PMD which is needed for sensory control of movement performance [14], and might support the notion that older subjects find the motor task more cognitively demanding. Increase of the activation is rather due to the change in gain settings, than threshold for activation [10].

DMN was shown to be heterogenous. Functional structure analysis of the DMN by the meta-analytic modeling showed several loops presence inside: PCC#MPFC#PCC and LIPL#RIPL, where the PCC has a 'hub' role [15]. MPFC is attributed to the emotional processing, while the parietal dorsolateral cortex controls the execution of motor tasks with increased attention need [16]. Presence of different subsystems in the DMN also was shown, assuming the MPFC and PCC as two core nodes, and medial temporal cortex - as quite different subsystem inside the DMN [17]. Also age differences in the strength of functional connectivity was shown, supporting evidence that DMN connectivity is particularly vulnerable to age [17]. Also evidence suggest that ageing leads to reduced after task functional connectivity and variability in the DMN [18]. As far as the DMN was found to be heterogenous, differences in age related functional connectivity withing some of the subsystems were found [17]. Stronger connectivity withing the MPFC in elderly was found, and weaker connectivity - withing heterogenous PCC (particularly its ventral and dorsal parts, the last has stronger connectivity in aged subjects, than ventral) [17]. We have found differences in DMN functioning during the motor task execution, particularly
DMN_{ind} and DMN_{deac}. The pattern of DMN deactivation in elderly was diminished in comparison to adult subjects, while the pattern of independent functioning of DMN was quite the same, including all the mentioned region, but with less extent of inclusion of each of them in elderly.
Images for this section:

**Fig. 2:** Regions of SMN activation in different age groups.

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**Fig. 3:** DMN deactivation pattern in Group 2 and Group 3.

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Fig. 4: Ratio of activation/deactivation volume in different agegroups.

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Conclusion

Greater activation in older subjects has referred to the increased need of the computational effort. The adaptable and plastic nature of the neural motor networks, explains the age-related changes in the brain. Thus, motor task fMRI activation pattern have age-related peculiarities. Depending on the age of the studied subject, evaluation of the fMRI activation pattern should be made taking into account described peculiarities. Activation-deactivation balance is seen only in the adult age, but not in young and elder subjects. DMN functional connectivity also shows age-dependent structure. Two modes of the DMN were shown to function during the movement execution in the adult age.
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