MOTOR SEQUENCE LEARNING: A FUNCTIONAL INTEGRATION STUDY IN FMRI

D. Coynel[1,2], V. Perlbarg[1,2], G. Marrelec[1,2], M. Pélégrini-Issac[1,2], S. Lehéricy[2,3], and H. Benali[1,2]

[1]UMR-S 678, Inserm and Université Pierre et Marie Curie, Faculté de médecine Pitié-Salpêtrière, Paris, F-75013, France, [2]IFR49 - Institut d'Imagerie Neurofonctionnelle, Gif-Sur-Yvette, F-91191, France, [3]Centre de NeuroImagerie de Recherche - CENIR, Université Pierre et Marie Curie, Paris, F-75013, France

Introduction

It has been proposed that motor sequence learning involves two distinct circuits, corresponding to the spatial and the motor representations of the sequence, respectively [1]. The motor associative (MA) circuit involves the frontoparietal cortices and the associative region of the basal ganglia (BG) and of the cerebellum (CB), while the sensorimotor (SM) circuit involves the motor cortices and the motor region of the BG and of the CB. According to this model, the representation of a motor sequence shifts from the MA to the SM loop during the learning process. This shift is made possible by the functional integration of MA and SM. In the present study, we tested this model by investigating the evolution of functional brain networks during motor sequence learning. Using fMRI data, we first extracted the motor network related to the learning task using a method based on spatial independent component analysis (ICA) similar to that proposed in [5]. We then used a measure called hierarchical integration [4] to follow the evolution of functional interaction within this network through learning.

Materials and methods

Motor learning protocol: The motor learning protocol lasted one month [2]. Twelve right-handed healthy volunteers practiced daily a sequence of eight moves using fingers 2 (index finger) to 5 (little finger) of the left hand. During fMRI sessions performed on days 1, 14, and 28, subjects had to perform the trained sequence, but also an untrained sequence which differed at each session, and a control sequence (2-3-4-5-2-3-4-5) where no learning is expected.

Extraction of functional networks: For each sequence type (trained/untrained/control) and fMRI session (day 1/14/28), we first performed an individual spatial ICA. The resulting spatial maps were then classified using a hierarchical clustering algorithm. Maps belonging to the same class were averaged, yielding a map representing a network that is reproducible across subjects. Among all such maps, the one corresponding to the motor network was identified and selected.

Functional connectivity: Seventeen regions of interest (ROIs) were defined from the spatial map of the motor network, using manually defined seed voxels and a local maximum search algorithm. Ten belonged to the MA network, and seven to the SM network. Mean time courses were extracted from these ROIs. Functional connectivity was measured with hierarchical integration, a quantity derived from mutual information [3] that can be interpreted in terms of functional interaction between regions or networks [4]. Here, we computed the integration within the motor network, as well as within the MA and the SM sub-networks, and between MA and SM.

Results and discussion

Extraction of functional networks showed that, on day 1, execution of the trained sequence involved bilateral associative and motor areas of the cortex, the BG and the CB, whereas on day 28 it mainly involved areas contralateral to the movement, and located in primary motor and premotor areas of the cortex, the BG and the CB (Fig. 1). These results were corroborated by the functional connectivity study: during the training period, from day 1 to day 28, integration of the motor network for the trained sequence significantly decreased (Student t-test, $p<.05$) from a value equivalent to that of the untrained sequence, to a value equivalent to that of the control sequence (Fig. 2). Similar changes were also found for MA and SM network integrations. Altogether, the changes observed in spatial structure and functional connectivity pattern suggest that the trained sequence is similar to the untrained sequence at the beginning of learning, while it becomes similar to the control sequence after learning.

The integration between MA and SM networks significantly decreased from day 1 to day 28 ($p<.05$) for the trained and control sequences, but not for the untrained sequence (Fig. 2). The variation relative to the control sequence may reflect habituation to the scanning environment as well as to the execution of the motor task. This also suggests that functional links between the two sub-networks are stronger during execution of a new sequence.

Conclusion

We proposed a novel approach to investigate functional brain networks using functional MRI data. Thanks to this framework, we demonstrated that learning induces changes in both the spatial structure of the motor network and its functional connectivity pattern.

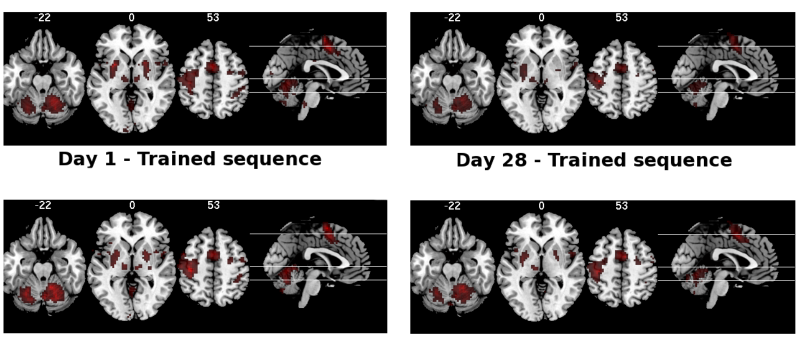

Fig.1: Spatial structure of the motor network

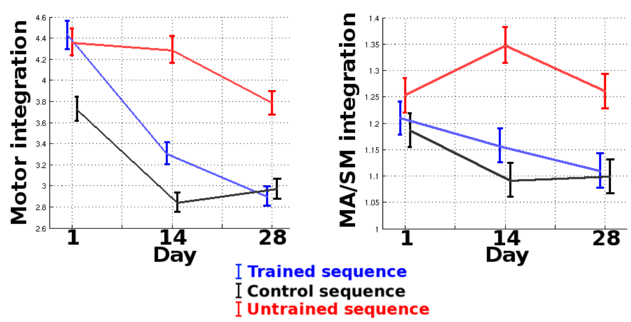

Fig. 2: mean value ± standard deviation of integration on day 1, 14, and 28

References

[1] Hikosaka *et al.*, *Curr. Opin. Neurobiol.*, 2002, **12**: 217-222; [2] Lehéricy *et al.*, *Proc. Natl. Acad. Sci. U.S.A.*, 2005, **105**: 12566-12571;
[3] Tononi *et al.*, *Proc. Natl. Acad. Sci. U.S.A.*, 1994, **91**: 5033-5037; [4] Marrelec *et al. Med. Image Anal.* (in revision); [5] Esposito *et al.*, *NeuroImage*, 2005, **25**: 193–205