Distinct regions of the basal ganglia are engaged in the early and late phases of learning

S. Lehericy[1], J. Doyon[2], H. Benali[3], P-F. Van de Moortele[1], T. Waechter[4], M. Pelegrini[5], K. Ugurbil[1]

[1]Center for Magnetic Resonance Research and Department of Radiology, University of Minnesota, Minneapolis, MN, United States, [2]Functional Neuroimaging Unit & Department of psychology, University of Montreal, Montreal, Canada, [3]Inserm U494, University of Paris 6, CHU Pitié-Salpêtrière, Paris, France, [4]Department of Neuroscience and Neurology, Brain Sciences Center, Minneapolis, MN, United States, [5]Inserm U483, University of Paris 6, CHU Pitié-Salpêtrière, Paris, France

Introduction. Previous studies suggest that anterior (associative) striatal regions are implicated during the acquisition of new motor skills, whereas the sensorimotor putamen may be critical for long-term storage (1,2). Thus, a shift of motor representations from the associative to the sensorimotor compartment of the basal ganglia during the course of motor sequence learning may be hypothesized. This hypothesis was examined using fMRI to track the time course of activation in the entire basal ganglia circuitry, as well as in other motor-related structures, during explicit learning of a sequence of finger movement over a month of training.

Material and methods. Fourteen healthy right-handed volunteers were studied with EPI BOLD contrast at 3T. Subjects had to practice 15 min daily over a period of 4 weeks a sequence of 8-moves using fingers 2 to 5 of the left hand. Subject's speed and accuracy were assessed weekly outside the scanner using a keyboard. Three MRI sessions were performed at day1, 14 and 28. Single shot oblique slices were obtained (TR/TE/angle: 4.5s/40ms/90°, in plane resolution: 1.5x1.5 mm^2, slice thickness 2.5 mm, no gap, 123 acquisitions, 43 slices). Movements were audio-paced at 2 Hz and alternated with rest. The same subjects performed sequences of identical length but different pattern for the unpracticed control state. Random effect group analysis was performed using SPM99 and individual post-hoc analysis using SPSS 11.5.

Results. After 4 weeks of training, subjects made 58% less errors and were 97% faster (ANOVA, all $p<0.05$). During fMRI sessions, reaction times decreased rapidly during the first run of Session1 and remained stable in all subsequent runs. There was no significant change for the untrained sequences.

Areas more activated during the early learning stage included bilateral preSMA, lateral premotor areas (PM), anterior cingulum, insula, parietal areas (BA 40 and precuneus), superior putamen and adjacent globus pallidus (GP), anterolateral thalamus, subthalamic nuclei (STN), red nuclei (RN), pons and cerebellum (lobules V,VI and crus I) (comparisons of the untrained versus trained sequences for each session, $p<0.001$). In the putamen, there were 2 main foci of activation located in the dorsal and more ventrolateral parts of the putamen body (Fig 1).
Regression analysis on percentage signal increase showed that activation decreased with practice in the dorsal part of both putamen ($R^2=0.64$, $p=0.030$, right putamen), whereas activation increased bilaterally in the ventral compartments ($R^2=0.67$, $p=0.046$). ANOVA for percentage signal increase showed a significant effect of the regions (ventral > dorsal putamen, $p=0.011$) and an interaction between runs and regions ($p=0.045$, Fig. 1 right).

Multiple regression analysis between signal variation and behavioral variables showed that 1) errors were positively correlated with areas activated during early learning (bilateral premotor, preSMA, dorsal putamen, and right parietal cortex at $p<0.001$, and bilateral STN and RN at $p<0.01$) and 2) reaction times were negatively correlated with areas activated during late learning stages (contralateral SMA posteroventral GP, ipsilateral cerebellum, RN, hippocampus, bilateral amygdala and orbitomedial frontal cortex at $p<0.001$, contralateral inferior putamen and RN and ipsilateral SN at $p<0.01$).

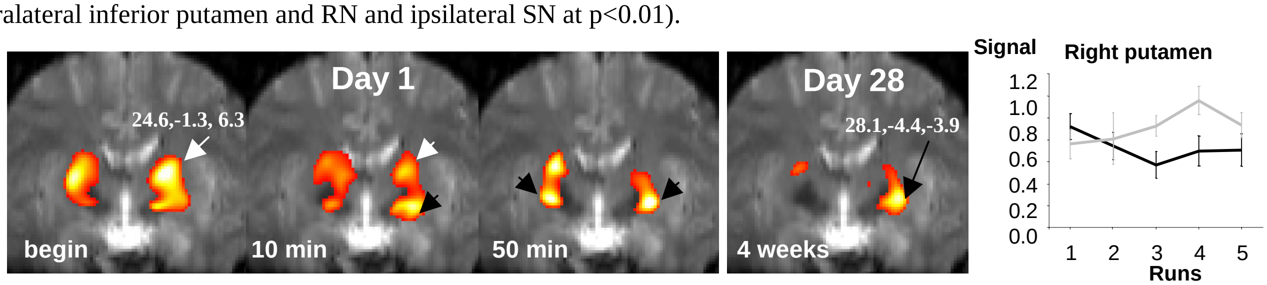

Figure 1. Activation maps obtained in the putamen superimposed on a coronal EPI images. There was a progressive activation decrease in the dorsal (associative) part of the putamen (white arrows) and an increase in a more ventrolateral area (black arrows) bilaterally which persisted at 4 weeks. Right: Percentage signal increase ± SEM averaged across all subjects for each run of the trained sequence in the dorsal (dark) and ventral (light grey) putamen.

Conclusion. These results show for the first time that there is a shift of motor representations from the associative to the sensorimotor compartment of the basal ganglia during the course of explicit learning of motor sequences.

References. (1) Jueptner et al. J Neurophysiol 1997, (2) Doyon et al. Proc Natl Acad Sci 2002.

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