February 21, 2018

Elife Editorial Office

Dear ,

Please find attached the manuscript "" by Pinsard, Boutin, Gabitov, Benali and Doyon, for consideration as a research article in Elife neuroscience category.

This article investigates the reorganization of the networks supporting the expression of newly acquired sequential skills after their consolidation using novel multivariate measures of fMRI BOLD activity patterns.

Research in neuroimaging, including work from our lab, have largely described non-linear evolution of brain regions activity levels along the course of motor sequence learning. Notably a reorganization of a network comprising cortical, cerebellar, hippocampal and striatal regions is observed when initial practice and retest sessions are separated by a sleep period during which reactivations of a subset of these regions occurs. While these changes show that complementary processes contributing to a more efficient practice are differentially at play in the course of learning, these does not necessarily reflect that all of this network encode the motor sequential knowledge, as these could also indicate a more general task knowledge. In fact, the tuning of local neuronal circuit were established to be measurable by fine-grained activity patterns of BOLD activity, notably by the group of Jörn Diedrichsen. However, in this seminal research, the sequence representations contrasted were either intensively trained over multiple days or newly practiced, the investigation was limited to dorsal cortical surface. Besides, the adopted approach was based on classifiers' performance with parametric statistical testing, a combination that was more recently shown to suffer from bias, and more adapted multivariate measure were since developed.

Therefore, we here wanted to investigate representational changes at a more focused and earlier stage of motor sequence learning that is the offline consolidation following regular practice. By measuring fine-grained activity evoked by the practice of two explicitly trained sequences of finger movements which underwent consolidation, as well as two similar newly acquired sequences, we were able to compute the unbiased continuous multivariate distance between these patterns over the whole brain with searchlight technique. We then assessed the prevalence of significant multivariate distances and their differences between learning stages across participants using non-parametric permutation testing. We here uncovered that large cortical regions representing new and consolidated sequences overlap, as well as a significant consolidation-induced reorganization of cortico-subcortical networks, showing that encoding of sequence in dorsomedial striatum and hippocampus are weakened while the representations in dorsolateral striatum, thalamus, cerebellum and secondary motor cortex are strengthened.

To conclude our results shows that among the regions dynamically recruited by the practice a sequential motor skill, only a part of those show plasticity of local neuronal circuits to encode the specific sequential information, and that some of these representations prevail at different time during learning. As we unveiled that striatal and hippocampal representation strengths change during consolidation, further work will be necessary to precisely investigate their geometry, notably whether respective egocentric and allocentric encoding can be assessed. Additionally, these results show the possibility to investigate knowledge-related representational changes appearing in an earlier phase of learning, notably by measuring adapted multivariate representational distances and statistical testing. Therefore, we think that Elife readers would be interested in these results that specify the functional roles of regions in motor plasticity, as well as the methodological approaches.

I remain at your disposal for any further information.

cover letter Elife guidelines :

How will your work make others in the field think differently and move the field forward? How does your work relate to the current literature on the topic? Who do you consider to be the most relevant audience for this work? Have you made

clear in the letter what the work has and has not achieved?

Sincerely yours,

Basile Pinsard
PhD candidate,
Laboratoire d'Imagerie Biomédicale, UMR S 1146 / UMR 7371, Sorbonne Universités, UPMC, INSERM, CNRS
Brain-Cognition-Behaviour Doctoral School, ED3C, UPMC, Sorbonne Universités
Biomedical Sciences Doctoral School, Faculty of Medicine, Université de Montréal
Centre de Recherche de l'Institut Universitaire de Gériatrie de Montréal