# Dynamic changes in whole-brain functional connectivity during story listening

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**Target Audience:** Researchers and clinicians who are interested in resting state fMRI (rs-fMRI) and dynamic functional connectivity. **Purpose:** Evidence from recent studies suggests that *Resting State Networks* (RSNs) change over space and time in relation to specific brain activities[1-3]. Indeed, during the execution of complex "continuous" cognitive tasks, such as listening to a narrated story, the brain elaborates information over multiple domains and time scales, integrating it across space and time[3]. These operations constantly contribute to shaping over time the whole-brain functional connectivity (FC). In this work we used rs-fMRI to investigate how large-scale functional interactions amongst RSNs dynamically change when subjects listen to a narrated story and assessed whether and how these changes influence the reorganisation of the brain's functional connectome. MRI acquisitions: 8 healthy subjects (mean age 39.62 ± 5.85) underwent MRI examination using a 3T MR Philips Achieva (Philips Healthcare, Best, The Netherlands). For each subject rs-fMRI images were acquired using a FFE-EPI sequence with TR/TE=4000/25 ms, voxel size=3x3x3.5 mm$^3$, FOV=230 mm, 43 slices, 120 volumes (total acquisition time=8.04 min). A 3D T1w scan was also collected with a FFE sequence (TR/TE=6.9/3.1ms; flip angle 5°; 180 slices; voxel size=1x1x1mm$^3$, FOV=256mm) for anatomical reference. Experimental design: a specific acquisition protocol with 4 consecutive rs-fMRI scans (labelled respectively: *PRE*, *STORY*, *POST1* and *POST2*) were performed to track FC changes in the RSNs in response to cognitive stimulation (narrated story), which was played during the entire duration of the 2nd rs-fMRI scan (*STORY*). The narrated story was 7 min in duration and contained specific features to stimulate certain cognitive processes including attention, working memory and visuo-spatial abilities. fMRI analysis: for each subject rs-fMRI images underwent Independent Component Analysis (ICA) to identify the RSNs (using MELODIC [FSL[4]]). We subsequently used the FSLNet[4] toolbox to perform functional connectome (*f-connectome*) modelling, considering each identified RSN as a "node" in the model. For each rs-fMRI run of the protocol, we computed the full correlation matrix to estimate the connection strengths among the nodes of the *f-connectome*. Finally, we applied a non-parametric permutation test (randomise) with 5000 permutations to statistically compare the group-specific correlation matrices. This step allowed detecting statistically significant changes occurring in the connection strengths (*edges*) among the nodes of the *f-connectome* within each of the 4 consecutive rs-fMRI runs of the protocol. **Results:** 14 RSNs were identified from Group-ICA analysis. All the RSNs dynamically changed FC magnitude and extension in relation to the story. In the *f-connectome* significant correlations ($p<0.05$) among the RSNs decreased in number and significance during and after the story, reaching a minimum number of significant interactions in *STORY* (see Fig.1). Furthermore, the initial RSN interactions (as shown in *PRE*), in particular those involving the sensorial networks such as the auditory network (AN), started to recover their interactions with other networks immediately in *POST1*, reaching an almost complete recovering in *POST2* (Fig.1). Cognitive RSNs, such as the salience (SN), the default mode (DMN), the task-positive (TPN), the cerebellum (CBLN) and the right ventral attention (RVAN) networks, responded to the listening task with long-term changes in their functional interactions, persisting with an altered condition in *POST2* (Fig.1). Moreover, during the *STORY*, the CBLN, RVAN and TPN showed their more complex web of interactions, striking new correlation *edges* with visual and attentional networks (see in Fig.1 the CBLN-MVN, TPN-MVN and RVAN-SN links). **Discussion and Conclusions:** Story listening provides a naturalistic stimulus during which complex cognitive tasks can be dynamically examined. We have shown that RSNs change their reciprocal functional interactions during story listening. These changes in RSNs modulate the *edges* of the *f-connectome* in a non-random way, with both short- and long-term effects. In particular, the changes in the shape of the *f-connectome* follow a hierarchical scheme of alterations that leads to affect sensorial RSNs (involved in the reception of the auditory input) prior in time than cognitive RSNs (involved in the understanding of the story contents). The results are consistent with selective changes in the assembly of networks occurring in response to changes in the stimuli that the brain receives. A possible interpretation is that the brain works as a *prediction engine*[5]. According to this idea, RSNs may be considered as multiple modes of constant inner state of exploration, in which the brain generates predictions about the configuration of the networks (as well as of the *f-connectome*) that would be optimal for a given impending input[5]. Furthermore, the increased complexity in the interaction web of the CBLN, RVAN and TPN during the story listening supports the idea that these networks play a relevant role in the attention switching from the internal to the external cognitive cues[6], passing through the internal visualization of the story scene. **Acknowledgements:** MS Society in UK, NIHR UCL-UCLH BRC, MSIF (Du Pré grant), the C. Mondino National Neurological Institute in Pavia (*5xmille,* year 2011) and the University of Pavia for grant funding. **References:** [1] Hao Jia (2014) *Brain Connect.* [2] Schlegel A (2013) *PNAS* 110(40): 16277-16282. [3] Berns GS (2013) *Brain Connect* 3(6): 590-600. [4] FSL, http://www.fmrib.ox.ac.uk/fsl. [5] Deco G (2011) *Nat Rev Neurosci* 12(1): 43-56. [6] Sidlauskaite J (2014) *Neuroimage* 98: 359-365.

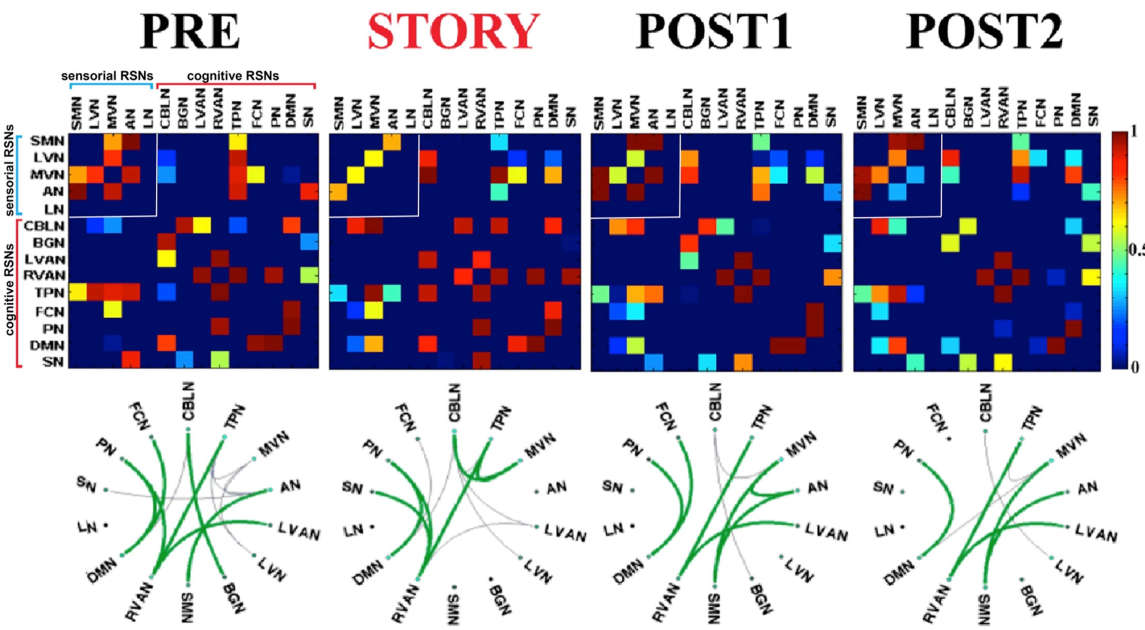


**Fig.1 –** Top: matrices of statistical significances (1-p) of *full* correlation strength among the 14 RSNs (nodes) of the *f-connectome* during the 4 rs-fMRI runs. Bottom: circular diagrams showing in *green* the most significant *edges* ($p \leq 0.05$) of the *f-connectome*. *Edges* for $0.05<p<0.1$ are shown in *grey*. Sensorial RSNs (top left of the matrices) responded to the listening task with short-term effects (mininum of *edges* in *STORY*). Cognitive RSNs responded to the stimulus with long-term effects (delayed effects in *POST1*).