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RESEARCH

RESTING STATE FUNCTIONAL CONNECTIVITY CHANGES IN NATURALISTIC STIMULATION STUDY

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Naturalistic stimulation has had increasing influence on cognitive neuroscience in the last decade. Several studies have used naturalistic stimulation to investigate the connectivity dynamics under pathological condition or in healthy children for studying the developing brain. However, little is known about the connectivity changes during watching a movie in healthy, adult population. Our aim is to delineate the potential dynamic connectivity pattern of the healthy, mature brain during naturalistic movie watching compared to complete rest. In an observational case series, eleven healthy adult volunteers with no history of psychiatric or neurological illness underwent two magnetic resonance echo-planar imaging acquisitions. During the first acquisition they were asked to rest with their eyes closed and during the subsequent acquisition they watched a movie clip with slow human body movements. The Independent Component Analysis provided neural components which were further submitted to intra- and inter-network analyses. We found significantly increased intra-network connectivity during movie watching for the extrastriate visual and for the posterior visual networks. The inter-network analysis showed that for the extravisual and primary visual pair, the connectivity was lower during movie watching compared to rest condition. We also found significant uncoupling between the anterior Default Mode Network and the secondary somatosensory network during movie watching. These findings suggest greater visual network segregation during movie watching in order to support processing of complex stimuli. The decoupling of the secondary somatosensory network from the anterior Default Mode Network during movie watching suggest a somatosensory function segregation and its important role in processing information from observing the naturalistic movements of others. Brain imaging measures of major brain networks can contribute to early identification of risk for common psychiatric disorders hence facilitating preventive therapy.

Keywords: naturalistic stimulation , rest, conectivity

INTRODUCTION

Brain neural dynamics can be evoked and captured, without making assumptions about their function, by an emerging technique called naturalistic stimulation. Naturalistic stimulation refers to complex dynamic stimuli such as movie watching. Watching a movie evokes reliable and functionally selective fluctuations in the BOLD signal throughout the brain, measurable using functional MR imaging (fMRI) [1][2][3]. Several benefits have been described in the literature for the naturalistic stimulation fMRI method.

Firstly, head motion reduction: head-motion is a common fMRI artifact particularly relevant among children, older adults and clinical populations [4][5]. Head motion can introduce significant, systemic effects on intrinsic functional connectivity measures during resting state-fMRI, specifically, head motion has been found to decrease functional coupling across long range connections while increasing local measures of functional coupling [6][7]. In contrast to the low behavioural constraint of conventional resting state, watching a movie in the MRI scanner has been shown to decrease subject movement [8][4], likely owing to viewers' enhanced attentional engagement [9].

Secondly, the increased intra-subject reliability of connectivity measures: the conventional resting state has been found to be quite dynamic as, during scanning, the level of awareness varies over time between wakefulness and different sleep stages [10] and these fluctuations can affect functional connectivity strengths in several networks. On the contrary, presenting a movie in the scanner has been shown to maintain wakefulness and attention in subjects [8]. Naturalistic stimulation improves intra-subject reliability relative to conventional resting state. Wang et al. demonstrated that movie viewing improves test-retest reliability, increasing the stability of functional connectivity measures by approximately 50% when compared to conventional resting-state paradigms [11]. All these benefits make natural stimulation a way for improving compliance, reducing movement and creating a more comfortable experience in the MR scanner for children, older adults and clinical population [9][12][8][3][5][4].

In the last years, several studies have been using naturalistic stimulation to investigate the connectivity dynamics under pathology condition (epilepsy, ADHD) or in healthy children for studying the developing brain [3][9][5].

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However, little is known about the connectivity changes during watching a movie in healthy, adult population. Our aim is to delineate the potential dynamic connectivity pattern of the healthy, mature brain functional networks during naturalistic movie watching compared to complete rest. Investigating these modulations in neural activity in healthy subjects would be informative for better understanding and interpreting the clinical data in naturalistic stimulation fMRI studies. Moreover, investigating the transition from complete rest to movie watching may be compelling as it can reflect a shift away from internally driven processing to external goal directed search like observing the naturalistic movements of others.

We sought to explore potential cerebral connectivity changes during naturalistic stimulation, in a hypothesis-free data driven fMRI technique.

MATERIALS ȘI METHODS

This study is an observational case series on healthy adult subjects. Eleven healthy volunteers (7 females, 4 males; average age, 33 years) with no history of psychiatric or neurological illness were selected from general population through an announcement on social networks. They underwent two fMRI echo-planar imaging acquisitions. During the first acquisition they were asked to rest with their eyes closed (Rest) and during the subsequent acquisition they watched a videoclip from a movie (Movie Watching, MW). The movie clip contained slow biological movements (human bodies movements). The Independent Component Analysis (ICA) method provided 50 independent component maps. Among them, 11 networks were identified as classical resting state neural networks, similar to those reported previously [13][14][15].

A 3T Siemens Skyra-MR scanner was used to acquire 200 functional axial volumes/session by means of a 2-dimensional multi-slice echo-planar imaging sequence (TR=2500 ms, TE=30ms, matrix=94x94, voxel size=4x4x4.3mm). Each acquisition duration was 8min43s. Additionally, anatomical images were acquired (T1-weighted MP-RAGE, TR/TE=2200/2.51 ms, voxel size 0.9x0.9x0.9 mm).

Data analysis was performed with FMRIB Software Library (FSL) package (http://fsl.fmrib.ox.ac.uk/fsl/fslwiki/). Head motion in the fMRI data was corrected using multi-resolution rigid body co-registration of volumes, as implemented in the MCFLIRT software. Brain extraction was carried out for motion corrected BOLD volumes with optimization of the deforming smooth surface model, as implemented in the BET software. Rigid body registration as implemented in the FLIRT software was used to co-register fMRI volumes to T1-MPRAGE (brain-extracted) volumes of the corresponding subjects and subsequently, to the MNI152 standard space. The images were smoothed with a 5 mm filter.

Independent Component Analysis (ICA). The Multivariate Exploratory Linear Decomposition into Independent Components (MELODIC) tool was used to perform spatial group-ICA using multisession temporal concatenation to produce 50 independent component maps (IC maps) representing average resting state networks. A high-pass temporal filtering cut-off of 100s was applied. The first 5 volumes, acquired to allow longitudinal magnetization to reach a steady state, were discarded.

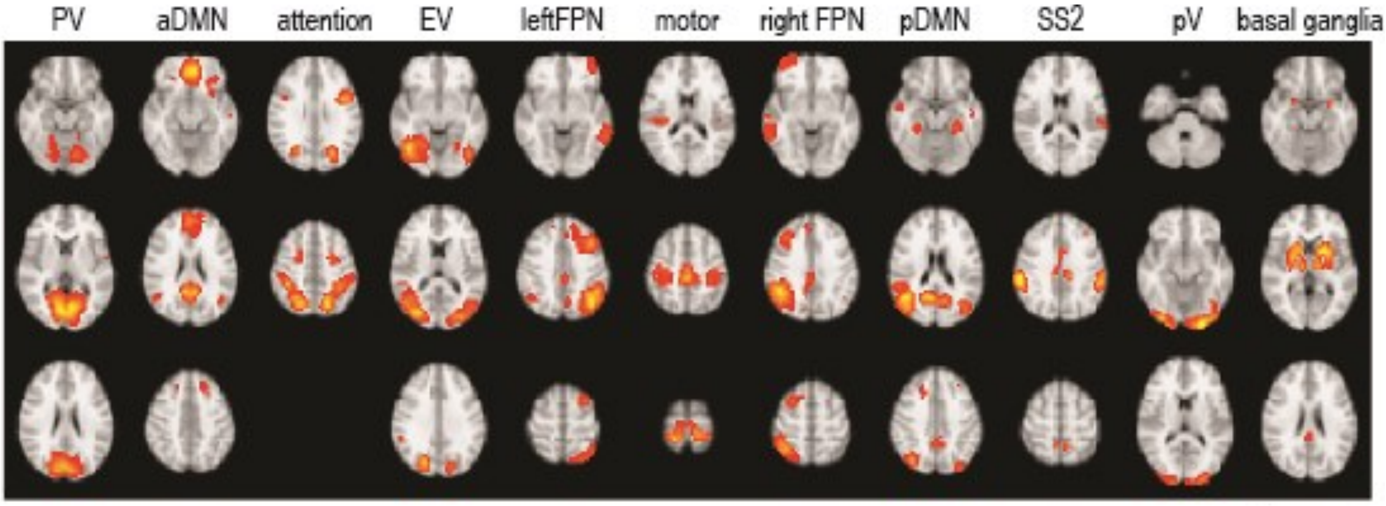
The **intra-network connectivity** analysis involves comparing the subject-specific spatial maps between Rest and MW conditions. To determine subject-specific spatial maps, dual regression analysis was performed on the obtained neural networks using variance normalization (with variance normalization, the dual regression reflects differences in both activity and spatial spread of the resting-state networks), similar to previous studies [3][15][14]. For the statistical analysis, i.e. the paired two-group difference (two-sample paired t-test), the different component maps were collected across subjects into single 4D files (1 per original ICA map) and tested voxel-wise by nonparametric permutation using the FSL randomise tool (https://fsl.fmrib.ox.ac.uk/fsl/fslwiki/Randomise) with 1000 permutations and a threshold-free cluster enhanced (TFCE) technique to control for multiple comparisons. As we tested a multitude of resting state networks in several runs, we addressed the issue of multiple testing correction by controlling the false discovery rate (FDR) at $p<0.05$.

Apart from testing differences for intra-network temporal correlation, we were interested in the potential changes of temporal correlations between resting state networks - **inter-network connectivity**. In order to obtain information on inter-network connectivity, we applied the FSLNets package (http://fsl.fmrib.ox.ac.uk/fsl/fslwiki/FSLNets) implemented in Matlab (The MathWorks Inc.).

In a preliminary step, the FSLNets tool performed an unsupervised grouping (clustering) of these networks to assess potential similarities and implicitly broad functional roles. Subsequently, we tested inter-network connection strength differences between conditions (Rest vs. MW condition). We considered as “good” (non-noise) temporal spectra only those which fall off smoothly with increasing frequency and which also fall to zero at the very lowest frequencies, due to highpass filtering applied in the preprocessing of the raw resting state-fMRI data. The remaining 11 networks were identified aș classical resting state networks (**Figure 1**). The FSLNets input data were the 22 (11x2) subject specific timecourses for the selected 11 neural networks (the timeseries outputs of stage 1 of the dual-regression). The group-ICA time-courses related to spatial maps were processed using the nets_load Matlab script implemented in FSLNets, which performs normalization for the overall standard deviation of all data points for each subject. These networks were further submitted to inter-network connectivity analysis. Then, subject-wise correlation matrices of both full correlation and regularized partial correlation of all remaining resting state networks time courses were created.

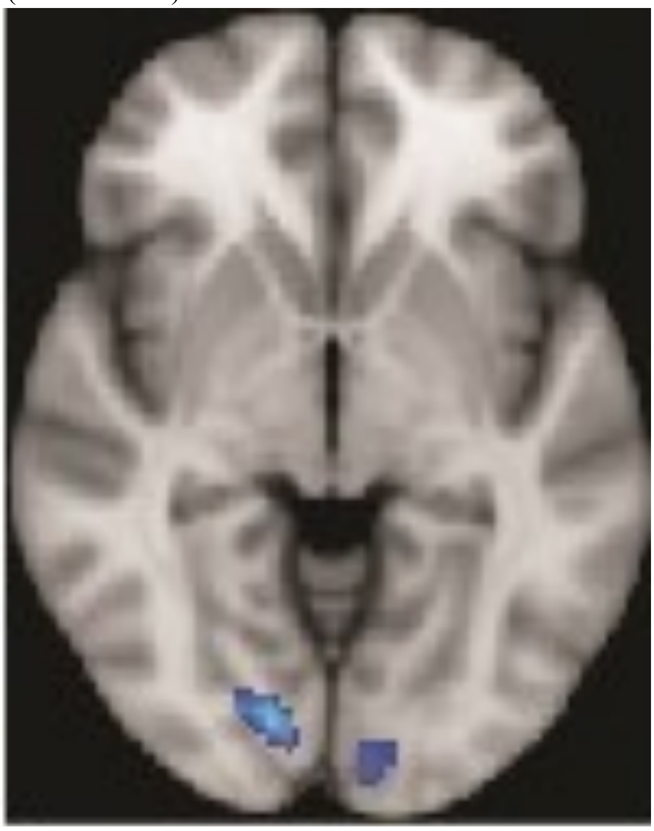
The resulting correlation coefficients were Fisher z-transformed and corrected for temporal autocorrelation. After averaging all individual correlation matrices and doing one-group t-test across them, the resulting nodes were clustered hierarchically by using information about temporal similarity of the full correlation matrices.

Figure 1: Independent Component Analysis (ICA) result (11 neural signal selected networks).



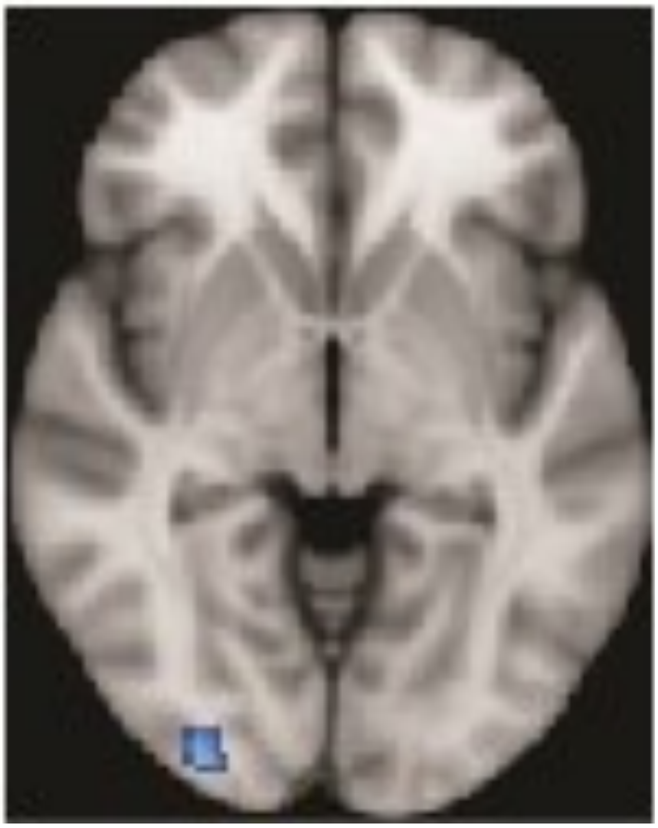
Legend: From left to right: primary visual network (PV), anterior DMN (aDMN), attention network, extrastriate visual network (EV), left fronto-parietal network (leftFPN), motor network, right fronto-parietal network (rightFPN), posterior DMN (pDMN), secondary sensory-motor network (SS2), posterior visual network (pV), basal ganglia network.

Figure 2: Cluster of voxels with increased connectivity (V2BA18 area)



Legend: Cluster of voxels with increased connectivity (V2BA18 area) (blue), during movie watching compared to rest, for the extrastriate network (p=0.0028).

Figure 3: Cluster of voxels with increased connectivity (V3V area)



Legend: Cluster of voxels with increased connectivity (V3V) (blue) during movie watching compared to rest, for the posterior visual network (p=0.0008).

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The network matrices were then tested across subjects for a two-group difference (Rest vs. MW condition). For group comparison we used a General Linear Model (GLM) on the partial correlation values, as these reflect direct network connections better than the full correlation values. Results were corrected for multiple testing by applying a family-wise error (FWE) correction, thresholded at p=0.05. The Juelich histological atlas, Harvard-Oxford cortical and subcortical atlases (Harvard Center or Morphometric Analysis) were used to identify the anatomical location and the NeuroSynth 100 top terms atlas (http://neurosynth.org) was used to identify the functional components of the resulting ICA maps.

RESULTS

Intra-network connectivity analysis

The whole brain comparisons of the component spatial maps performed by dual-regression revealed significantly increased intra-network connectivity during MW compared to Rest condition, for the extrastriate visual network (EV) and for the posterior visual network (pV). The extrastriate visual network encompasses mainly higher-order, processing cortical visual areas while the posterior visual network comprises both primary and higher-order visual areas. The clusters of voxels showing increased connectivity during MW are located bilaterally in visual cortex V2BA18 (part of EV network)(**Figures 2 and 1**) and in visual cortex V3V (part of pV) (**Figures 3 and 1**). We found no other significant differences in intra-network connectivity during MW compared to Rest.

Inter-network connectivity analysis

The inter-network analysis performed by FSLNets showed that the inter-network connectivity changed significantly for the EV and primary visual (PV) pair, between Rest and MW condition. For this functional node, the inter-network connectivity was higher during Rest compared to MW (Figure 4). More specifically, the EV and PV networks had a strong positive correlation during Rest but they almost completely lose their correlation during MW (Figure 4).We also found significant connectivity modulation between the anterior Default Mode Network (aDMN) and the secondary somatosensory network (SS2) (**Figure 5**). A weak anti-correlation during Rest for this functional pair became a strong anti-correlation during MW.

DISCUSSIONS

The naturalistic experimental stimulation have had increasing influence on cognitive neuroscience in the last decade [16][3][8][9][1][17][4]. Now, naturalistic paradigms have a place in the Human Connectome Project (HCP) (http://www.humanconnectomeproject.org) and the Healthy Brain Network (HBN) [18]. A recent review in Trends in cognitive science, "Naturalistic Stimuli in Neuroscience: Critically Acclaimed", praise the role of naturalistic stimulation in cognitive neuroscience.

In recent years, the focus was shift from regional brain abnormalities to dysfunction or abnormal connectivity in brain's networks, in the efort to find explanatory models for various neuropsychiatric disorders, from autism and ADHD to schizophrenia and depression [19]. For instance, negative connectivity was found in high-visual network and executive network coupling in schizophrenic patients and their first-degree relatives and this decreased connectivity was correlated with the severity of positive symptoms in patients [20]. The application of a low level natural stimulation like movie watching has been used in resting state studies in order to investigate potential connectivity changes induced by disease [9][3][8] or to study young children's functional brain systems. Emerson et al. applied this method in 6 year-old children in order to investigate the normal development of the cortex [3]. In another study, Bullen use ICA method to investigate alterations between Rest and MW induced by epilepsy pathology [9].

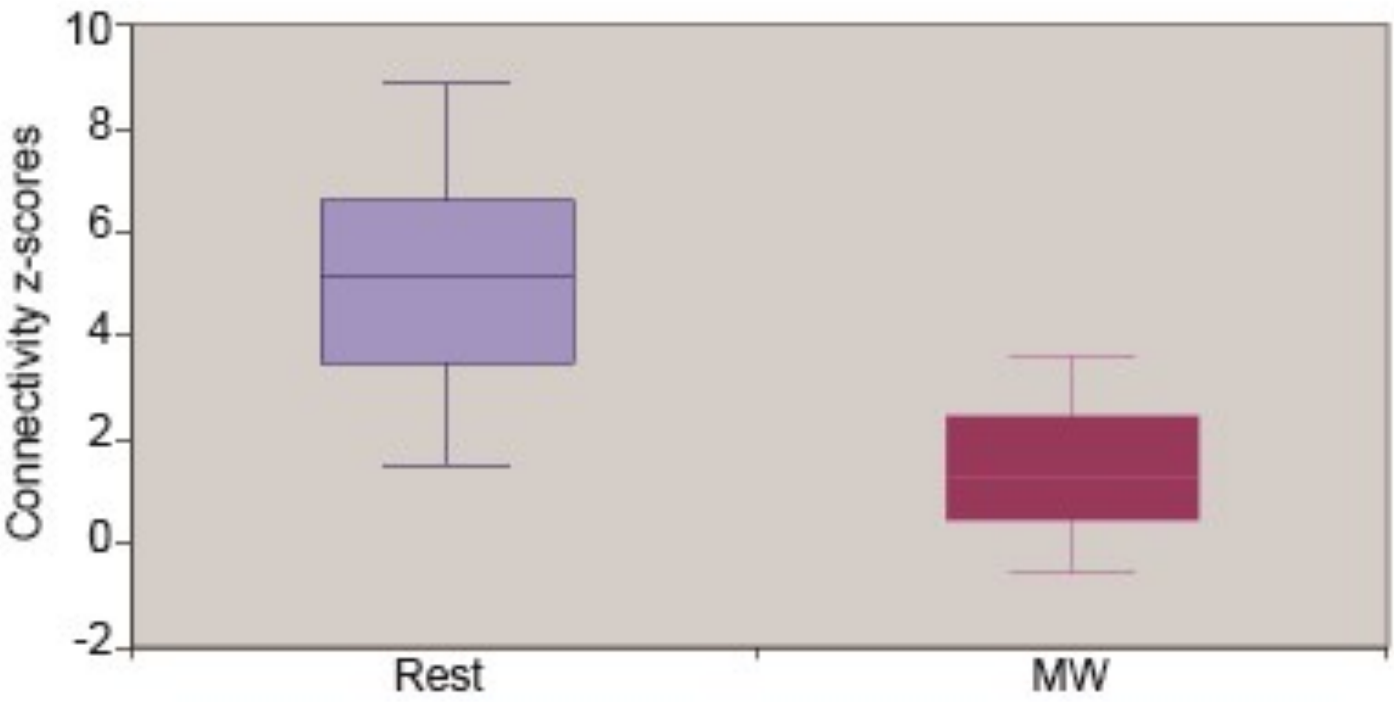
However, very few studies have investigated the changes in neural connectivity from Rest to MW brain states in healthy volunteers. To the best of our knowledge, only one other group, Gao and Lin, performed this kind of investigation on healthy adults [16]. In order to explore the neural connectivity changes, Gao and Lin used predefined spherical regions of interest positioned inside several resting state-fMRI networks provided by a different study. In our study, we used an unsupervised data analysis (ICA) in order to obtain our own group neural networks. Subsequently, these networks were used for checking intra- and inter-network connectivity potential changes during MW compared with Rest.

The intra-network analysis showed increased connectivity for two visual networks. To the best of our knowledge, the only other analysis of intra-network connectivity during naturalistic stimulation was performed by Emerson et al in 6-year old children. They did not obtain differences for the intra-network connectivity but their study involved young children. We found increased intra-network connectivity for EV network and posterior visual network during MW compared to Rest. The voxels proving stronger intra-network connection were located in prestriate and striate areas (V3 and, respectively, V2 areas) which are known to be sensitive to shape dynamics. V2 area is part of the associative visual cortex with functions involving visual discrimination, visual memory, etc.. V3 area may play a role in the processing of global motion [21].

These intra-network, local increases in connectivity during naturalistic stimulation suggest a segregation of functional networks in order to support movie processing [9]. Other studies [22][23] support our findings as they found processing hubs (i.e. higher local, intra-network connection) during movie viewing, demonstrating greater network segregation during active engagement.

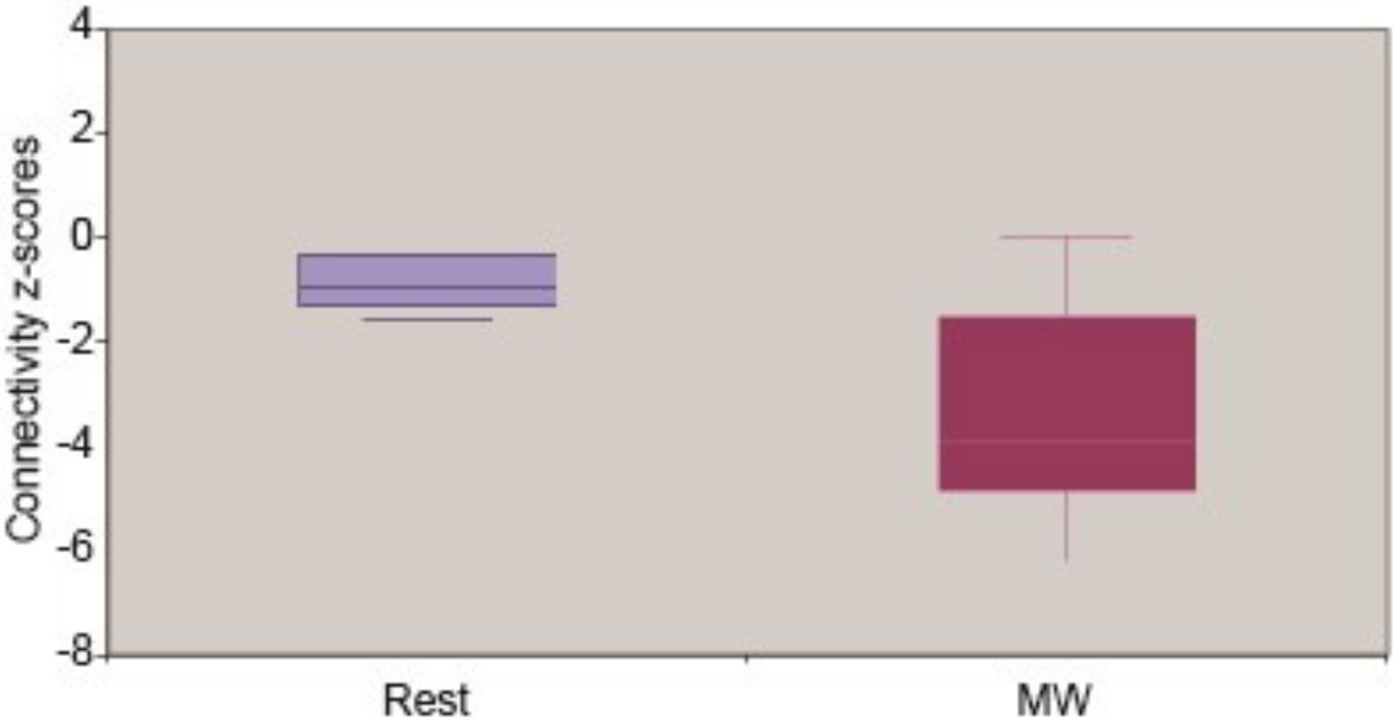
Our study proved significantly decreased inter-network connectivity between extrastriate and primary visual networks during MW. This finding is in agreement with Bullen study which found that the most weakened inter-network connectivity is between extrastriate visual (EV) network and primary visual (PV) network during MW [9].

Figure 4: The boxplots of connectivity z-scores between secondary somatosensory and anterior default mode network, in rest and movie watching conditions.



Legend: Significantly lower positive correlation between networks during movie watching.

Figure 5: The boxplots of connectivity z-scores between secondary somatosensory and anterior default mode network, in rest and movie watching conditions



Legend: Significantly higher anti-correlation between networks during movie watching.

Bartels et al. also found that distinct visual areas lose their correlations during MW compared to Rest [1]. McAvoy and colleagues reported the dissociated mean BOLD signal changes between PV and EV regions, in an experiment with participants alternating between fixation and eyes closed [24]. Their study concludes that a dissociated endogenous neural activity in PV and EV cortices may represent a general aspect of brain function when shifting from internally to externally directed states [24]. Similarly, in our study, the naturalistic stimulation seems to produce a segregation between EV network and lower order visual networks. The intra-network connectivity increase along with the inter-network connectivity decrease for the these visual areas suggest a stronger local activity and a weaker long-range connectivity during MW compared to Rest.

The second result of the inter-network analysis is the uncoupling (strong anti-correlation) between aDMN and SS2 during MW (**Figure 5**). We identified SS2 location in accordance to Juelich atlas implemented in FSLeyes (GM parietal operculum, bilateral). It had been believed that SS2 cortex is a unimodal sensory cortex that contributes to the processing of tactile information and of proprioceptive information for motor control. However, electrophysiological studies as well as more recent fMRI studies often demonstrate the existence of bimodal neurons in this area [25]. Recent human brain-imaging studies have often demonstrated visual effects on SS2 activity. Bremmer et al. studied the motion processing system in the human brain using fMRI and found that moving visual stimulation activated SS2 [26]. The activation of the SS2 by the observation of another person's body being touched has been repeatedly confirmed under various conditions [27][28]. Even viewing another person's actions can activate SS2 [29][30][27]. A recent study performed in macaque monkeys which recorded single-unit (neuron) activity with intracranial electrodes, found that among 1157 recorded neurons in SS2, 306 neurons (~26.5%) responded to visual stimuli [25]. These visual neurons responded rather complex stimuli such as observation of human action and moving-object stimulation outside the monkey's reach. The visual neurons were distributed continuously along the lateral sulcus covering the entire SS2, along with other somatosensory neurons [25].

In our study, the SS2 anti-correlation with aDMN become very strong when toggling from Rest to MW, suggesting a dissociation of SS2 from other networks and a higher local processing of external stimuli like pictures of body movements. The high anti-correlation between the SS2 network and aDMN might be explained by a competitive relationship between them [31][32]. The fact that only aDMN and not pDMN showed this connectivity modulation with SS2 during MW might be explained given that aDMN is more prone than pDMN to reflect the relation between others and oneself and is activated during thinking about the complex interactions among people [33][34]. The Default mode network (DMN) is one of the most studied brain networks, due to its association with almost every major psychiatric disease. In depression and schizophrenia, the DMN was found to be hyperactivated and hyperconnected. In schizophrenia these abnormalities is thought to be responsible for the intensive self-reference and also for the impairments in attention and working memory. In depression, DMN hyperactivity is associated with negative rumination [35]. In the last years many leading professionals proposed that brain imaging measures can contribute to early identification of risk for common psychiatric disorders and resting-state fMRI represents a promising biomarker for the early identification of children at risk of developing depression or ADHD, hence facilitating preventive therapy [36].

To conclude, we found several features of the brain processes during a low demand naturalistic stimuli: higher intra-network connectivity and lower inter-network connectivity for the visual areas suggesting greater network segregation during MW in order to support processing of complex stimuli. We also found a strong uncoupling of the SS2 and aDMN networks during MW, suggesting a SS2 function segregation and an important role for SS2 in processing information from observing the naturalistic movements of others.

Study limitations:

We performed our study comparing the eyes closed resting state to movie watching condition. This method has been previously used by Gao and Lin and by Bullen in their naturalistic stimulations studies [16][9]. However, there are previous studies that suggest that connectivity changes are present when just switching from eyes closed to eyes open condition. Indeed, larger activation for the visual areas are reported in Marx et al. study in eyes open than in eyes shut condition [37][38][39]. On the other hand, there are studies that found no significant differences in connectivity strength for the important networks, between eyes open and eyes closed conditions [40].
While the increased connectivity inside visual areas in our naturalistic stimulation study might be similar to those found for eyes open condition in other studies, the finding related to SS2 and DMN uncoupling during movie watching has not been previously reported by other eyes shut/eyes open studies so this strong anti-correlation might be a potential feature for the brain while observing other people movements. Further studies comparing eyes open fMRI to movie watching condition are necessary to confirm the present findings on the neural response to movie watching, specifically, while observing the movements of others.

References:

1. Bartels Andreas, and Semir Zeki. 2005. "Brain Dynamics during Natural Viewing Conditions--a New Guide for Mapping Connectivity in Vivo." *NeuroImage* 24 (2): 339–49.
2. Hasson, Uri, Galia Avidan, Hagar Gelbard, Ignacio Vallines, Michal Harel, Nancy Minshew, and Marlene Behrmann. 2009. "Shared and Idiosyncratic Cortical Activation Patterns in Autism Revealed under Continuous Real-Life Viewing Conditions." *Autism Research: Official Journal of the International Society for Autism Research* 2 (4): 220–31.
3. Emerson R.W., Short S.J., Lin W. Gilmore J.H., Gao W. 2015. „Network-Level Connectivity Dynamics of Movie Watching in 6-Year-Old Children." *Front Hum Neurosci.* 9:631
4. Vanderwal, Tamara, Clare Kelly, Jeffrey Eilbott, Linda C. Mayes, and F. Xavier Castellanos. 2015. "Inscapes: A Movie Paradigm to Improve Compliance in Functional Magnetic Resonance Imaging." *NeuroImage* 122 (November): 222–32
5. Huijbers, Willem, Koene R. A. Van Dijk, Meta M. Boenniger, Rüdiger Stirnberg, and Monique M. B. Breteler. 2017. "Less Head Motion during MRI under Task than Resting-State Conditions." *NeuroImage* 147: 111–20.
6. Power, Jonathan D., Kelly A. Barnes, Abraham Z. Snyder, Bradley L. Schlaggar, and Steven E. Petersen. 2012. "Spurious but Systematic Correlations in Functional Connectivity MRI Networks Arise from Subject Motion." *NeuroImage* 59 (3): 2142–54
7. Van Dijk, Koene R. A., Mert R. Sabuncu, and Randy L. Buckner. 2012. "The Influence of Head Motion on Intrinsic Functional Connectivity MRI." *NeuroImage* 59 (1): 431–38
8. Centeno, Maria, Tim M. Tierney, Suejen Perani, Elhum A. Shamshiri, Kelly StPier, Charlotte Wilkinson, Daniel Konn, et al. 2016. "Optimising EEG-FMRI for Localisation of Focal Epilepsy in Children." *PloS One* 11 (2): e0149048.
9. Bullen, Alenka. 2017. "Movie-Driven FMRI Reveals Network Asynchrony and Connectivity Alterations in Temporal Lobe Epilepsy." *Electronic Thesis and Dissertation Repository*, August.
10. Tagliazucchi, Enzo, and Helmut Laufs. 2014. "Decoding Wakefulness Levels from Typical FMRI Resting-State Data Reveals Reliable Drifts between Wakefulness and Sleep." *Neuron* 82 (3): 695–708.
11. Wang, Jiahui, Yudan Ren, Xintao Hu, Vinh Thai Nguyen, Lei Guo, Junwei Han, and Christine Cong Guo. 2017. "Test-Retest Reliability of Functional Connectivity Networks during Naturalistic FMRI Paradigms." *Human Brain Mapping* 38 (4): 2226–41.
12. Barnea-Goraly, Naama, Stuart A. Weinzimer, Katrina J. Ruedy, Nelly Mauras, Roy W. Beck, Matt J. Marzelli, Paul K. Mazaika, et al. 2014. "High Success Rates of Sedation-Free Brain MRI Scanning in Young Children Using Simple Subject Preparation Protocols with and without a Commercial Mock Scanner--the Diabetes Research in Children Network (DirecNet) Experience." *Pediatric Radiology* 44 (2): 181–86.
13. Smith, Stephen M., Peter T. Fox, Karla L. Miller, David C. Glahn, P. Mickle Fox, Clare E. Mackay, Nicola Filippini, et al. 2009. "Correspondence of the Brain's Functional Architecture during Activation and Rest." *Proceedings of the National Academy of Sciences* 106 (31): 13040–45.
14. Werner, Cornelius J., Imis Dogan, Christian Saß, Shahram Mirzazade, Johannes Schiefer, N. Jon Shah, Jörg B. Schulz, and Kathrin Reetz. 2014. "Altered Resting-State Connectivity in Huntington's Disease." *Human Brain Mapping* 35 (6): 2582–93.
15. Onu, Mihaela, Liviu Badea, Adina Roceanu, Madalina Tivarus, and Ovidiu Bajenaru. 2015. "Increased Connectivity between Sensorimotor and Attentional Areas in Parkinson's Disease." *Neuroradiology* 57 (9): 957–68
16. Gao, Wei, and Weili Lin. 2012. "Frontal Parietal Control Network Regulates the Anti-Correlated Default and Dorsal Attention Networks." *Human Brain Mapping* 33 (1): 192–202.
17. Pamilo, Siina, Sanna Malinen, Yevhen Hlushchuk, Mika Seppä, Pia Tikka, and Riitta Hari. 2012. "Functional Subdivision of Group-ICA Results of FMRI Data Collected during Cinema Viewing." *PLOS ONE* 7 (7): e42000.
18. Sonkusare, Saurabh, Michael Breakspear, and Christine Guo. 2019. "Naturalistic Stimuli in Neuroscience: Critically Acclaimed." *Trends in Cognitive Sciences* 23 (8): 699–714.
19. Konrad, Kerstin and Eickhoff, B. Simon.2010. "Is the ADHD brain wired differently? A review on structural and functional connectivity in attention deficit hyperactivity disorder". *Hum Brain Mapp* 31(6): 904-916
20. Li, Peng, Fan, Teng-Teng, Zhao, Rong-Jiang, Han, Ying, Shi, Le …and Lu, Lin. 2017. "Altered Brain Network Connectivity as a Potential Endophenotype of Schizophrenia". *Scientific Reports* 7 (5483)
21. Braddick, Oliver J, Justin M D O'Brien, John Wattam-Bell, Janette Atkinson, Tom Hartley, and Robert Turner. 2001. "Brain Areas Sensitive to Coherent Visual Motion." *Perception* 30 (1): 61–72.
22. Moussa, Malaak Nasser, Crystal D. Vechlekar, Jonathan H. Burdette, Matt R. Steen, Christina E. Hugenschmidt, and Paul J. Laurienti. 2011. "Changes in Cognitive State Alter Human Functional Brain Networks." *Frontiers in Human Neuroscience* 5: 83
23. Cohen, Jessica R., and Mark D'Esposito. 2016. "The Segregation and Integration of Distinct Brain Networks and Their Relationship to Cognition." *The Journal of Neuroscience: The Official Journal of the Society for Neuroscience* 36 (48): 12083–94

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24. McAvoy, Mark, Linda Larson-Prior, Marek Ludwikow, Dongyang Zhang, Abraham Z. Snyder, Debra L. Gusnard, Marcus E. Raichle, and Giovanni d'Avossa. 2012. "Dissociated Mean and Functional Connectivity BOLD Signals in Visual Cortex during Eyes Closed and Fixation." *Journal of Neurophysiology* 108 (9): 2363–72.
25. Hihara, Sayaka, Miki Taoka, Michio Tanaka, and Atsushi Iriki. 2015. "Visual Responsiveness of Neurons in the Secondary Somatosensory Area and Its Surrounding Parietal Operculum Regions in Awake Macaque Monkeys." *Cerebral Cortex* 25 (11): 4535–50.
26. Bremmer, Frank, Anja Schlack, N. Jon Shah, Oliver Zafiris, Michael Kubischik, Klaus-Peter Hoffmann, Karl Zilles, and Gereon R. Fink. 2001. "Polymodal Motion Processing in Posterior Parietal and Premotor Cortex: A Human FMRI Study Strongly Implies Equivalencies between Humans and Monkeys." *Neuron* 29 (1): 287–96
27. Keysers, Christian, Bruno Wicker, Valeria Gazzola, Jean-Luc Anton, Leonardo Fogassi, and Vittorio Gallese. 2004. "A Touching Sight: SII/PV Activation during the Observation and Experience of Touch." *Neuron* 42 (2): 335–46
28. Keysers, Christian, Jon H. Kaas, and Valeria Gazzola. 2010. "Somatosensation in Social Perception." *Nature Reviews. Neuroscience* 11 (6): 417–28.
29. Agnew, Zarinah, and Richard J. S. Wise. 2008. "Separate Areas for Mirror Responses and Agency within the Parietal Operculum." *The Journal of Neuroscience: The Official Journal of the Society for Neuroscience* 28 (47): 12268–73.
30. Gazzola, Valeria, Lisa Aziz-Zadeh, and Christian Keysers. 2006. "Empathy and the Somatotopic Auditory Mirror System in Humans." *Current Biology: CB* 16 (18): 1824–29.
31. Fox, Michael D., Abraham Z. Snyder, Justin L. Vincent, Maurizio Corbetta, David C. Van Essen, and Marcus E. Raichle. 2005. "The Human Brain Is Intrinsically Organized into Dynamic, Anticorrelated Functional Networks." *Proceedings of the National Academy of Sciences* 102 (27): 9673–78.
32. Fransson, Peter. 2005. "Spontaneous Low-Frequency BOLD Signal Fluctuations: An FMRI Investigation of the Resting-State Default Mode of Brain Function Hypothesis." *Human Brain Mapping* 26 (1): 15–29.
33. Buckner, Randy L., and Daniel C. Carroll. 2007. "Self-Projection and the Brain." *Trends in Cognitive Sciences* 11 (2): 49–57.
34. Buckner, Randy L., Jessica R. Andrews Hanna, and Daniel L. Schacter. 2008. "The Brain's Default Network." *Annals of the New York Academy of Sciences* 1124 (1): 1–38.
35. Whitfield-Gabrieli, Susan and Ford, M. Judith. 2011. "Default Mode Network Activity and Connectivity in Psychopathology" *Annual Review of Clinical Psychology* 8(1):4
36. Whitfield-Gabrieli, Susan, Wendelken, Carter, Nieto-Castañón, Alfonso et al. 2020. "Association of Intrinsic Brain Architecture With Changes in Attentional and Mood Symptoms During Development" *JAMA Psychiatry 77(4): 378-386*
37. Marx, Esther, Angela Deutschländer, Thomas Stephan, Marianne Dieterich, Martin Wiesmann, and Thomas Brandt. 2004. "Eyes Open and Eyes Closed as Rest Conditions: Impact on Brain Activation Patterns." *NeuroImage* 21 (4): 1818–24.
38. Marx, Esther, Thomas Stephan, Annina Nolte, Angela Deutschländer, Klaus C. Seelos, Marianne Dieterich, and Thomas Brandt. 2003a. "Eye Closure in Darkness Animates Sensory Systems." *NeuroImage* 19 (3): 924–34.
39. Marx, Esther, Thomas Stephan, Annina Nolte, Angela Deutschländer, Klaus C Seelos, Marianne Dieterich, and Thomas Brandt. 2003b. "Eye Closure in Darkness Animates Sensory Systems." *NeuroImage* 19 (3): 924–34.
40. Patriat, Rémi, Erin K. Molloy, Timothy B. Meier, Gregory R. Kirk, Veena A. Nair, Mary E. Meyerand, Vivek Prabhakaran, and Rasmus M. Birn. 2013. "The Effect of Resting Condition on Resting-State FMRI Reliability and Consistency: A Comparison between Resting with Eyes Open, Closed, and Fixated." *NeuroImage* 78 (September): 463–73.