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Dynamic Functional Connectivity Captures Individuals' Unique Brain Signatures

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Abstract. Recent neuroimaging evidence has emerged suggesting that there exists a unique individual-specific functional connectivity pattern consistent across tasks. The objective of our study is to utilize functional connectivity patterns to identify an individual using a supervised machine learning approach. To this end, we use two previously published data sets that comprises resting-state and task-based fMRI responses. We use static functional connectivity measures as input to a linear classifier to evaluate its performance. We additionally extend this analysis to capture dynamic functional connectivity using two approaches: the common sliding window approach and the more recent phase synchrony-based measure. We found that the classification models using dynamic functional connectivity patterns as input outperform their static analysis counterpart by a significant margin for both data sets. Furthermore, sliding window-based analysis proved to capture more individual-specific brain connectivity patterns than phase synchrony measures for resting-state data while the reverse pattern was observed for the task-based data set. Upon investigating the effects of feature reduction, we found that feature elimination significantly improved results upto a point with near-perfect classification accuracy for the task-based data set while a gradual decrease in the accuracy was observed for resting-state data set. The implications of these findings are discussed. The results we have are promising and present a novel direction to investigate further.

Keywords: fMRI · functional connectivity · classification · variance inflation factor · individual differences

1 Introduction

Neuroscience has progressed by leaps and bounds in the past two decades. A growing interest to understand the structure and function of the brain has resulted in significant advancements in both data acquisition and analyses techniques. Central to one of the most common efforts to decipher brain function is functional magnetic resonance imaging (fMRI), an indirect measurement of the neuronal activity.

Recent studies, however, have questioned the effectiveness of fMRI in understanding brain function and predicting future brain activity (although these studies primarily dealt with task based fMRI)[1][2] . Other studies have also shown that functional networks are dominated by stable individual features independent of task [3]. Gratton et al.[3] reported that an individual's brain network is dominated by stable group and individual factors while using a static functional connectivity approach(sFC). This would then imply that sFC patterns would represent an individual's functional connectivity signature thereby allowing us to identify an individual across tasks. However, it remains to be seen if this applies in a naturalistic paradigm wherein the participant performs a contiguous task like movie viewing[7] or music listening[8] thereby emulating real-life experiences. Moreover, Gratton et al. did not investigate individual-specific dynamic functional connectivity(dFC) patterns. Some of the most common approaches used are sFC analyses[4], and dFC analyses like Correlation-based Sliding Window (CSW) analysis [5] and the more recent Instantaneous Phase Synchrony (IPS) analysis[6].

The sFC analysis approach involves taking an average of the time series for region of interest(a voxel or parcel) and using this for further analysis with the primary assumption that networks are temporally stationary. While this leads to an ease in result interpretability, the primary problem encountered is the loss of the temporal dimension shifting the focus entirely to the spatial dimension.

Dynamic functional connectivity, on the other hand, incorporates temporal fluctuations, a clear improvement over it's static counterpart. In its most basic version, the CSW dynamic approach uses a sliding window of a fixed length in order to capture temporally varying functional networks. IPS is a novel approach introduced quite recently into fMRI based studies[10]. This method compares the phase angles for each brain voxel or region (depending on the area of interest) at every single time point thus providing the same temporal resolution as the original fMRI data. Another study has found CSW and IPS to convey comparable information[11], where IPS is preferred as it foregoes the need to select appropriate window length and overlap required for CSW. It remains to be seen as to which of these techniques captures individual-specific information better.

The main objective of our study is to identify individuals based on their functional connectivity patterns. To this end, we try to glean a functional signature from their sFC and the two dFC approaches. Subsequently, we compare the classification accuracy so as to determine the stronger approach. In order to assess the external validity of the proposed classification approach, we use two different datasets. Building on that, we have performed experiments to identify individuals based on their fMRI scans using 2 different data sets. One, a passive task based music listening data set(part of "Tunteet" data set), and the other a resting state data set(part of HCP data set). The passive music listening task is part of the naturalistic paradigm, so as to emulate real-life listening situations in addition to being comparable to resting-state while performing the task (music listening). This would help us in understanding whether a unique FC signature exists for a participant and whether it can be replicated over time. As far as we know, this is the first study to attempt identifying participants based on their intrinsic static and dynamic functional connectivity signatures.

2 Methods

The study was performed on two different data sets which were previously used in already published research papers. The first one, part of the data sets uploaded in the "Human Connectome Project", is a resting state data set[14] (henceforth referred to as the "HCP data set"). The second one, part of "Tunteet" data set, is a passive task based music listening data set[12, 13] (henceforth referred to as the "musical data set"). Both the data sets were chosen for their difference between each other and their history of being used previously in published studies.

2.1 Data Set Specification

HCP data set: This data set consists of resting state fMRIs of 40 random participants from the much larger HCP1200 Young Adult data set[14] so as to keep it comparable to the musical data set. Each scan was 15 minutes long, done twice for every participant with a gap of 3 weeks. The subjects were asked to be at rest and think about nothing while undergoing the fMRI scan. The subjects were processed with the HCP minimal preprocessing pipeline[15]). More details can be found in the HCP documentation page[20].

Musical data set: The first set consisted of 36 participants, that included 18 musicians (9 females, age 28.2 ± 7.8 years) and 18 non-musicians (10 females, age 29.2 ± 10.7 years). All the participants were asked to listen to three instrumental pieces - Stream of Consciousness by Dream Theater (progressive rock), Adios Nonino by Astor Piazzolla (tango nuevo), and the first three dances of the Rite of Spring by Igor Stravinsky (modern classical). Each piece was roughly around 8 min long and belonged to a different genre.

The brain responses of participants were acquired while they listened to the musical stimuli presented in randomized order. Their only task was to attentively listen to the music delivered via MR-compatible insert earphones while keeping their eyes open. The data was preprocessed using well-established preprocessing methods[7].

2.2 Feature Extraction

The fMRI data from both the data sets were first parcellated using the AAL atlas which resulted in time-series of 116 regions to ease the computations required in the tasks ahead.

Static Functional Connectivity: For correlation-based static Functional Connectivity matrices (sFC), pair-wise Pearson correlation coefficients were calculated between the brain regions for the time series from each scanning session. This resulted in a symmetrical correlation matrix of size $116 \times 116 \times 2$ for every participant in the HCP data set, and $116 \times 116 \times 3$ for every participant in the musical data set. These matrices were converted to vectors by linearizing the lower-triangular matrix without the diagonal, resulting in $\frac{116\times115}{2} = 6670$ feature vector for every scanning session. This resulted in a feature set of size 6670×80 for the HCP data set, and 6670×108 for the musical data set.

Dynamic Functional Connectivity:

Correlation-based Sliding Window. For this analysis, a rectangular window of size 10 time points with 50% overlap was employed as shown in Fig. 1. Pair-wise Pearson correlation was performed between the brain regions with all the time-points in a single window for every scanning session. The resultant 116×116 matrices were then linearized using the same method as used in sFC analysis. This was done for all the participants in both the data sets, which resulted in $6670 \times \omega1 \times 40$ feature set for every scanning session for the HCP data set, and $6670 \times \omega2 \times 36$ feature set for every stimulus in the musical data set, where $\omega1$ *and* $\omega2$ are the total number of windows for every participant in the HCP and musical data set respectively.

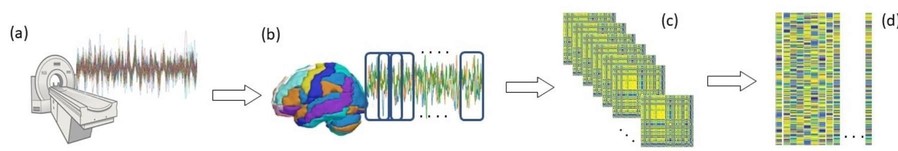


Fig. 1: For CSW analysis, every participant's data goes through the following steps: (a) Voxel based time series. (b) Parcellation into 116 regions and 50% overlapping window of 10 time points. (c) Region-wise correlation and generation of CSW matrices for every time window. (d) Linearization of lower triangular matrix for every time point to get a 2D matrix per participant per scanning session.

Instantaneous Phase Synchrony. As shown in Fig. 2, Hilbert transform was applied on the parcellated fMRI time series of every region for every participant to get the analytical signal, upon which phase angle was calculated. Then cosine of instantaneous phase angle difference was calculated between every pair of regions for all the time points which resulted in a 116×116 symmetrical distance matrix for every time-point. These IPS matrices were linearized using the same method as used for sFCs for every participant generating a dynamic IPS, resulting in $6670 \times \tau1 \times 40$ feature set for every scanning session for the HCP data set, and $6670 \times \tau2 \times 36$ feature set for every stimulus in the musical data set, where $\tau1$ *and* $\tau2$ are the total number of time points for every participant in the HCP and musical data set respectively.

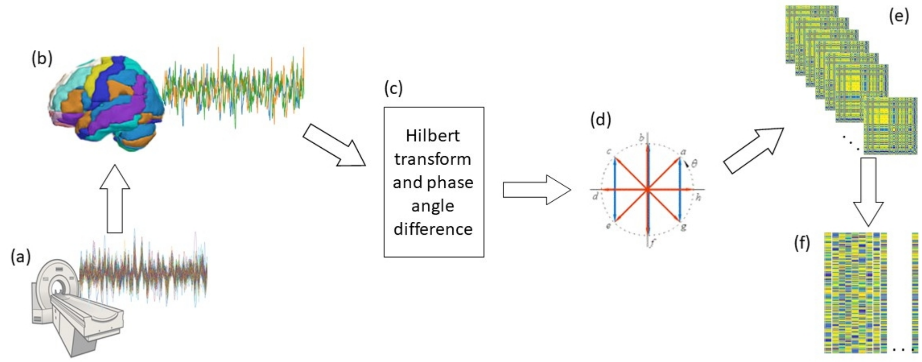


Fig. 2: For IPS analysis, every participant's data goes through the following steps: (a) Voxel based time series. (b) Parcellation into 116 regions. (c) Hilbert transform, phase angle calculation and region-wise angular difference. (d) cosine function on outcome of c. (e) IPS matrices for every time point. (f) Linearization of lower triangular matrix for every time point to get a 2D matrix per participant.

2.3 Classification

We used Linear Discriminant Analysis (LDA) from python's scikit-learn toolbox[16] for classification as it is a parameter-free method and is a simple model that is easy to interpret. The classification tasks were performed separately on both sets of data and both sets of static and dynamic matrices generated from the data sets. For the HCP data set, the classification accuracy was calculated using the feature set from the first scanning session for training the model and from the second scanning session done 3 weeks later for testing. The classification accuracy in musical data set was tested using leave-one-stimulus-out cross validation method for each stimulus, and a 50% cross validation method. For the first cross validation method, time points from two stimuli were used for training the classification models and the time points from the remaining stimulus were used for validation, where the cross validation methods would be denoted henceforth as S1, S2, and S3 for using Dreamtheater, Piazzolla, and Stravinsky scans for validation respectively. For 50% cross validation method, half of the time points from each stimulus were used for training and the other half were used for testing.

The classification accuracy for dynamic analyses were evaluated using two different techniques. For the first method, classification accuracy for classification of every time window was calculated for CSW (CSW-TW), and accuracy for classification of every time point in IPS (IPS-TP). For the second method, a majority voting method was applied to measure the overall classification accuracy of participants. In this technique, we take a majority vote of all the classes the time windows or time points for each participants are classified in, and the participants are classified in the class in which maximum number of their time points are classified. This method will be denoted by CSW-MV and IPS-MV for both the dynamic analyses.

2.4 Feature elimination

In order to reduce the dimensionality of the feature set owing to potential multicollinearity, the Variance Inflation Factor (VIF) technique was used to identify a unique set of features from the original feature set. Variance Inflation Factor (VIF) is a technique used to evaluate multicollinearity in a set of regression variables[17], using which we repetitively eliminated the features with maximal multicollinearity among all the features at every iteration until we get the desired size of the feature set. The features identified using VIF feature elimination do not necessarily guarantee greater classification accuracy since it is purely a data-driven approach; however, it allows us to identify the contribution of subsets of the input feature set that provided us with the best classification accuracy for each data set.

For HCP data set, VIF elimination was performed on the training set of CSW as it had provided us with the best results. The feature set was reduced to 50%, 30%, 15%, 10%, 5%, and 1% of the original feature set and the remaining features were used to train and test the LDA classifier and classification accuracy was calculated. For the musical data set, VIF elimination was performed on the training set of IPS as it provided the best results. The feature set upon which VIF was to be performed was the one used for 50% cross validation method as it included time points from all three stimuli. The feature set was reduced to the same number of features as for the HCP data set and the resultant features were used to train and test the LDA classifier for all three of the S1, S2, and S3 cross validation methods.

3 Results

3.1 Classification

Overall, dynamic analyses approaches provided far better accuracy in classifying individuals than the static ones, as it can be observed in Table 1, which contains the classification results on the complete feature set. The classification accuracy on classification using CSW-MV was found to be most significant for the HCP data set with an accuracy score of 0.775. Whereas for the musical data set, classification accuracy for IPS-TP provided far better classification accuracy at an average of 0.8148 across all cross validation methods. This was also the highest classification accuracy found in classification among all the data sets and types of analyses.

For classification using IPS for the musical data set, the classification model performs varyingly for different cross-validation methods. Table 2 gives a summary of classification results on the musical data set for all cross validation methods using the LDA classifier on the IPS data.

Table 1: Overall classification accuracy for both data sets with different feature extraction techniques using complete feature set.

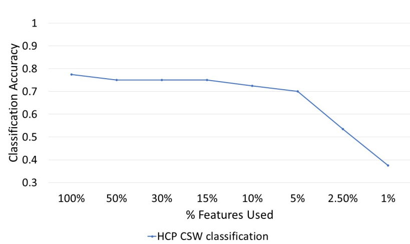
Data set	sFC	CSW-TW	CSW-MV	IPS-TP	IPS-MV
HCP 40	0.1625	0.386	0.775	0.2730	0.45
Musical	0.4814	0.2541	0.7129	0.3437	0.8148

Table 2: Cross-validation results using LDA classifier on IPS data of musical data set.

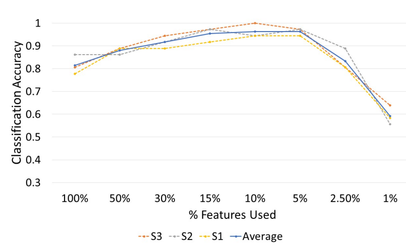
Cross validation method	IPS-TP	IPS-MV
50% Cross validation	0.335	0.9444
Leave Dreamtheater out	0.344	0.7778
Leave Piazzolla out	0.3508	0.8611
Leave Stravinsky out	0.3365	0.8056

3.2 VIF Feature Elimination

As seen in Fig. 3a, upon implementing VIF elimination for the the HCP data set, the participant classification accuracy reduced as the number of features were reduced, while the sharpest drop in accuracy was seen on using the feature set with 2.5% of the original features. The accuracy trend for classification of IPS data in musical data set with different number of features and using different cross-validation methods can be seen in Fig. 3b for participant classification accuracy. Here, the overall participant classification accuracy increased as the number of features were reduced until it reached a peak on using 10% of the feature set (667 features from the original 6670 feature set), and the classification accuracy started decreasing again on using 2.5% features from the original feature set.



(a) HCP data set classification scores trend



(b) Musical data set classification scores trend

Fig. 3: VIF Feature Elimination based classification score trend

4 Discussion and Scope

Across both data sets, it was observed that dFC feature-based classification models outperformed their sFC counterpart. This supports the notion that the temporal dimension indeed captures nuanced individual-specific signatured brain organization patterns. The CSW approach exhibited comparable classification accuracies of around 70% accuracy in both datasets which is significantly higher than chance level, that is, 2.5% (1/40) for HCP and 2.8% (1/36) for Music datasets respectively. This is a notable result in particular for the HCP dataset since there exists a time lapse of three weeks between the acquisition of both rsfMRI sessions. This in fact indicates that short time periods, at least limited to weeks do not engender stark differences in brain functioning which manifest in fMRI data. CSW-based classification approach outperformed IPS-based classification for the HCP dataset while the opposite trend was observed for the musical dataset. Specifically, a 10% increase in accuracy was observed in the Music dataset as a result of the IPS-based classification. This can be attributed to the fact a rich stimulus like music requires an individual to process several elements in parallel such as melody, rhythm, timbre, and tonality in parallel, which are known to recruit large-scale networks with overlapping regions and hence would be captured better with a measure such as IPS. Additionally one could postulate that an external stimulus such as music evokes rapid temporal changes in brain states that cannot be so accurately captured with a sliding window approach.

Furthermore, music processing and experienced emotional states have been found to be modulated by several individual factors such as musical expertise, personality, empathy[18, 19], which further potentially manifests as distinct synchronization between specific brain regions at an individual level. This would then allow us to postulate that IPS is more representative of dynamic brain functioning than the CSW approach as it captures minuscule changes owing to its ability to integrate data from a smaller timescale than CSW. The majority vote approach turned to be a more accurate approach for classification than the individual time-point classification approach. This implies that there indeed exist common dynamic FC patterns/states across individuals and hence a minimum number of observations per participant is required for successful classification. This calls for further investigation.

The feature elimination process resulted in differing trends in both datasets. While reduced number of features resulted in a decrease in classification accuracy in the HCP dataset, an increase in the classification accuracy approaching near-perfect classification (with top 5% = 333 features) was observed for the music dataset before evidencing a declining trend. A similar steep decrease was observed post 5% of the feature set related to the HCP dataset. The decrease in accuracy for the HCP dataset might imply that all pair-wise connection patterns are essential when using the CSW-approach. On the other hand, the increasing classification accuracy of the classification model for the musical data as a result of VIF feature elimination can be attributed to the removal of noise from the feature set thereby improving the overall quality of data. In fact, certain regions in the brain have been found to consistently process certain musical features across individuals[18], which, when removed, allows to better find intrinsic functional networks. However, it remains to be seen which regions con-tribute the most in correctly classifying the participants with a higher accuracy. This calls for a focused study in feature importance for classification, which is beyond the scope of the current study. In fact, identifying specific regions, the phase synchronization of which would be important in classifying individuals, would be valuable in contexts wherein severity of neurological conditions such as autism or mental health conditions such as depression, post-traumatic stress disorder, need to be predicted.

This work can be naturally extended to investigate other tasks such as naturalistic viewing, reading, language processing, to check whether IPS does outperform CSW consistently across multiple tasks, especially in the same set of individuals. Furthermore, dFC-based features may be subjected to other classification models to compare performance while keeping in mind complexity and interpretability of the model. A concern with CSW is the lack of consensus on window length. Shorter windows are likelier to capture noise in the data while longer windows would generate more accurate results at the cost of temporal resolution. The effect of removal of global regression of data and the effect of band-pass filtering (also based on the frequency range) of data before IPS also has to be investigated, but our ongoing pilot study using these steps in the feature extraction part has provided notably similar results. The AAL atlas used in the current study sacrifices a lot of spatial resolution for ease of computation, so a higher resolution atlas should also be looked into to investigate the spatial scales at which the individual brain networks differ.

References

1. Botvinik-Nezer, R., Holzmeister, F., Camerer, C.F. et al. Variability in the analysis of a single neuroimaging dataset by many teams. Nature 582, 84–88 (2020). https://doi.org/10.1038/s41586-020-2314-9
2. Elliott, M. L., Knodt, A. R., Ireland, D., Morris, M. L., Poulton, R., Ramrakha, S., ... Hariri, A. R. (2020). What Is the Test-Retest Reliability of Common Task-Functional MRI Measures? New Empirical Evidence and a Meta-Analysis. Psychological Science. https://doi.org/10.1177/0956797620916786
3. Gratton C, Laumann TO, Nielsen AN, et al. Functional Brain Networks Are Dominated by Stable Group and Individual Factors, Not Cognitive or Daily Variation. Neuron. 2018;98(2):439-452.e5. doi:10.1016/j.neuron.2018.03.035
4. Biswal, B.; Zerrin Yetkin, F. Z.; Haughton, V. M.; Hyde, J. S. (1995). "Functional connectivity in the motor cortex of resting human brain using echo-planar MRI". Magnetic Resonance in Medicine. 34 (4): 537–541. doi:10.1002/mrm.1910340409
5. Hutchison, R. M.; Womelsdorf, T.; Allen, E. A.; Bandettini, P. A.; Calhoun, V. D.; Corbetta, M.; Della Penna, S.; Duyn, J. H.; Glover, G. H.; Gonzalez-Castillo, J.; Handwerker, D. A.; Keilholz, S.; Kiviniemi, V.; Leopold, D. A.; De Pasquale, F.; Sporns, O.; Walter, M.; Chang, C. (2013). "Dynamic functional connectivity: Promise, issues, and interpretations". NeuroImage. 80: 360–378. doi:10.1016/j.neuroimage.2013.05.079

6. Enrico Glerean, Juha Salmi, Juha M. Lahnakoski, Iiro P. Jääskeläinen, and Mikko Sams: "Functional Magnetic Resonance Imaging Phase Synchronization as a Measure of Dynamic Functional Connectivity". Brain Connectivity. Apr 2012. 91-101. http://doi.org/10.1089/brain.2011.0068
7. Hasson U, Nir Y, Levy I, Fuhrmann G, Malach R. Intersubject synchronization of cortical activity during natural vision. Science. 2004;303(5664):1634-1640. doi:10.1126/science.1089506
8. Alluri V, Toiviainen P, Jääskeläinen IP, Glerean E, Sams M, Brattico E. Large-scale brain networks emerge from dynamic processing of musical timbre, key and rhythm. Neuroimage. 2012;59(4):3677-3689. doi:10.1016/j.neuroimage.2011.11.019
9. Yeo BT, Krienen FM, Sepulcre J, Sabuncu MR, Lashkari D, Hollinshead M, Roffman JL, Smoller JW, Zollei L., Polimeni JR, Fischl B, Liu H, Buckner RL. The organization of the human cerebral cortex estimated by intrinsic functional connectivity. J Neurophysiol 106(3):1125-65, 2011.
10. Omidvarnia, A., Pedersen, M., Walz, J.M., Vaughan, D.N., Abbott, D.F. and Jackson, G.D. (2016), Dynamic regional phase synchrony (DRePS). Hum. Brain Mapp., 37: 1970-1985. doi:10.1002/hbm.23151
11. Pedersen M, Omidvarnia A, Zalesky A, Jackson GD. On the relationship between instantaneous phase synchrony and correlation-based sliding windows for time-resolved fMRI connectivity analysis. Neuroimage. 2018;181:85-94. doi:10.1016/j.neuroimage.2018.06.020
12. Burunat I, Brattico E, Puoliväli T, Ristaniemi T, Sams M, Toiviainen P: (2015) Action in Perception: Prominent Visuo-Motor Functional Symmetry in Musicians during Music Listening. PLoS ONE 10(9): e0138238. https://doi.org/10.1371/journal.pone.0138238
13. Alluri V, Toiviainen P, Burunat I, Kliuchko M, Vuust P, Brattico E. Connectivity patterns during music listening: Evidence for action-based processing in musicians. Hum Brain Mapp. 2017;38(6):2955-2970. doi:10.1002/hbm.23565
14. David C. Van Essen, Stephen M. Smith, Deanna M. Barch, Timothy E.J. Behrens, Essa Yacoub, Kamil Ugurbil, for the WU-Minn HCP Consortium. (2013). The WU-Minn Human Connectome Project: An overview. NeuroImage 80(2013):62-79.
15. Matthew F. Glasser, Stamatios N. Sotiropoulos, J. Anthony Wilson, Timothy S. Coalson, Bruce Fischl, Jesper L. Andersson, Junqian Xu, Saad Jbabdi, Matthew Webster, Jonathan R. Polimeni, David C. Van Essen, and Mark Jenkinson (2013). The minimal preprocessing pipelines for the Human Connectome Project. Neuroimage 80: 105-124.
16. Pedregosa, F., G., Varoquaux, A., Gramfort, V., Michel, B., Thirion, O., Grisel, M., Blondel, P., Prettenhofer, R., Weiss, V., Dubourg, J., Vanderplas, D., Passos, M., Brucher, M., Perrot, and E., Duchesnay: "Scikit-learn: Machine Learning in Python".Journal of Machine Learning Research 12 (2011): 2825–2830.
17. Snee, Ron. (1981). Who Invented the Variance Inflation Factor?. 10.13140/RG.2.1.3274.8562.
18. Alluri V., Toiviainen P., Lund T., Wallentin M., Vuust P., Nandi A., Ristaniemi T., and Brattico, E. (2013). From Vivaldi to Beatles and back: predicting brain responses to music. Neuroimage. 83, 627-636. doi: 10.1016/j.neuroimage.2013.06.064
19. D Niranjan, I Burunat, P Toiviainen, E Brattico, V Alluri. Influence of Musical Expertise on the processing of Musical Features in a Naturalistic Setting. 2019 Conference on Cognitive Computational Neuroscience. https://doi.org/10.32470/CCN.2019.1314-0
20. Human Connectome Project Homepage, http://www.humanconnectomeproject.org. Last accessed 15 Jun 2020