Minimum spanning tree in analyzing audiovisual integration network: A developmental study

Abbas Pourhedayat[1], Shahriar Gharibzadeh[2], Fatemeh Bakouie[3,*]

1 Institute for Cognitive & Brain Sciences, Shahid Beheshti University, Tehran, Iran.

Address: 1983963113, Daneshjou Boulevard, District 1, Tehran, Tehran, Iran.

Orcid: 0000-0002-6232-0734, Email: a_pourhedayat@sbu.ac.ir

Tel: +98-2129905405, Mobile: +98-9116434979

2 Institute for Cognitive & Brain Sciences, Shahid Beheshti University, Tehran, Iran.

Address: 1983963113, Daneshjou Boulevard, District 1, Tehran, Tehran, Iran.

Orcid: 0000-0002-9604-8433, Email: s_gharibzadeh@sbu.ac.ir

Tel: +98-2129905405, Mobile: +98-9121947863

3 Institute for Cognitive & Brain Sciences, Shahid Beheshti University, Tehran, Iran.

Address: 1983963113, Daneshjou Boulevard, District 1, Tehran, Tehran, Iran.

Orcid: 0000-0002-6625-8720 , Email: f_bakouie@sbu.ac.ir, fatemeh.bakouie@gmail.com

Tel: +98-2129905405, Mobile: +98-9111551862

[*] **Corresponding author**:

Fatemeh Bakouie, PhD.

Abstract

Audiovisual integration (AVI) is a brain function that combines received information from visual and auditory sources. Delay in the development of multisensory integration functions makes functional problems in cases like autism spectrum disorder. However, the nature of the development of its network in the brain is poorly understood. We used resting-state functional magnetic resonance imaging data from ADHD 200 publicly available dataset. There are 192 records from typically developing children (92 Girls) in open eyes conditions which we used to make AVI networks based on functional connectivities. The minimum spanning tree tool was used to have comparable networks. We explored the measures of the extracted trees to discover changes in the developmental trajectory. The links of the AVI network undergo many changes before nine years and nine months, which form the main structure of the network. Most of these changes in links are related to the superior parietal gyrus area. The subsequent changes are related to setting the network performance, most of which are intra-regional links related to the superior temporal gyrus. Based on our results, it is recommended to perform localization tasks for rehabilitation or enhancement of AVI in the early stages of AVI development.

Keywords: Audiovisual integration, Development, Graph theory, Resting state fMRI, Functional connectivity, Minimum spanning tree.

1. Introduction

The brain combines information received through different sensory modalities to gain more information [1]. The process of combining the auditory and visual information is called audiovisual integration (AVI) [2]. This function improves reaction times in response to audiovisual (AV) stimuli, makes localization of the AV source more accurate, and results in better speech comprehension [3–6].

Studies have shown that some disorders like autism make defects in this function [7–9]. People with autism show delays in reaching optimal state in the function of the AVI compared to normal adults [10]. As a result, the pattern of the AVI development in typically developed people can help us to find out the nature of the defects [11]. Accordingly, researchers designed studies on how and when people start to benefit from AVI [12]. They compared different groups of children during development. Based on different methods used and the age range, they declared different ages as starting times of the AVI [12,13]. Researchers have shown that children do not benefit from the AVI before the age of 7, and they used switching strategy between two senses [14]. By development, signs of the presence of AVI in individuals have been reported [14–16]. By reaching the ages of 10 to 11, the performance of individuals approaches to adults' one [15]. Subsequently, the process of AVI evolves with the growth [17]. Concerning the broad age range used in these studies, it cannot be sure about its starting time [12]. In addition, the different used tasks in studies made it hard to reach the same viewpoint. Moreover, different tasks activated various areas during doing tasks [18–20]. These variations also affect the reported relationship between areas [21]. In studies that examine localizing the AV stimuli, researchers reported the activity of the superior parietal gyrus (SPG) [22,23]. In examining the AV temporal judgment, the superior temporal gyrus (STG) shows more activity [23–25]. While both of these conditions, activate AVI to process. Researchers have shown that the AVI depends on the dynamics of the relationship between areas [26]. Therefore, finding the changes that lead to individuals benefiting from AVI requires the involved areas to be studied simultaneously.

Graph theory (GT) is a computational tool that provides a holistic perspective about networks [27,28], like the audiovisual integration network (AVIN). Using GT and network science makes it possible to examine the involved areas and changes in communication between them [28–30]. In addition, it is possible to study the AVI independently of tasks and in a resting state.

Using GT for studying the brain networks of individuals with different ages is facing some challenges. One challenge is the non-uniform distribution of participants in different groups. The statistical method of bootstrap has been proposed to address the issue of comparing the groups of participants with non-uniform distribution. It makes possible to compare age groups in brain network studies. In this method, a subset of data is obtained using resampling, which diminishes the impacts of the subject-specific networks with different patterns of connections on results [31].

Different density of network links is the other challenge in network comparison between groups that can yield spurious results [32–34]. This difference in links density affects the extracted measures from networks and makes the results incomparable. There are various methods to address this issue, one of which is the Minimum Spanning Tree (mST). The mST is a sub-network that connects all network nodes without creating a loop [34,35]. It is consisted of links that make total links weight minimum possible. Previous studies has shown the mST will be unique if the network has distinct weights, like the brain networks. Also, it retains the dynamics and features of the main network while eliminating methodological biases in network comparison [34]. These advantages have made mST as a suitable tool for comparing networks with different densities, such as brain networks.

In brain studies, we typically use neuroimaging data representing the strength of connectivities. Therefore, examining brain networks requires to use the Maximum Spanning Tree (MST) [34]. In this case, the link selection process follows a way that maximizes the sum of weights. In this case, the link selection process follows a way that maximizes the sum of weights. It has been shown that MST has a similar performance to mST [34,36]. In recent years, various studies have used MST tool in the field of brain networks studies to compare individuals' networks in different groups and conditions [36–38].

For this purpose, in this study, we used resting-state fMRI data to extract and evaluate the AVIN. We hypothesize that using network science tools can reveal changes in brain areas associated with AVI. Also, by comparing the information obtained from AVIN and previous studies, it is possible to say what kind of changes make AVIN functional in individuals during development. Comparing networks of children at different ages requires an unbiased way to compare networks [33,34]. As a result, we used the maximum spanning tree tool, making it possible to reach this aim.

2. Material and methods

2.1 Data resource

The objective of this research is to study changes in AVIN during development. Therefore, we used a publicly available rs-fMRI dataset called ADHD-200. The anonymous dataset is freely available through the internet address link (http://fcon_1000.projects.nitrc.org/indi/adhd200/index.html#; RRID:SCR_005358) [39]. This dataset contains information of 598 typically developing participants and 374 patients with diagnosed attention deficit hyperactivity disorder. Data has been recorded in a resting state with open or closed-eyes conditions. Participants' ages range is from 7 to 23 years, most of whom were under 14 years old. We used preprocessed dataset through the NIAK pipeline for this study (http://neurobureau.projects.nitrc.org/ADHD200/Introduction.html; RRID:SCR_000576). We used the version with a 1000 mm3 threshold in the parcellation phase, which has 954 regions of interest (ROIs) for whole brain. So, there are 954 time series for each participant, which are the average time series of the existing voxels in each ROI [40,41].

To AVIN extraction, we needed recorded data from participants who had received both auditory and visual sensory inputs simultaneously. Therefore, just data recorded in the opened-eye condition were used to make AVIN. Records of typically developed right-handed individuals were extracted using the demographic dataset, which included 192 participants (92 F).

2.2. AVIN extraction

We must extracted the relevant parcels to the areas involved in AVI from 954 ROIs of whole brain to define the nodes of AVIN. Table 1 shows the related information to the involved areas (Figure 1A) and their equivalent parcels in the ALL Atlas we used in this research [42]. Each parcel which more than 50% of its volume involved in AVI areas was coded with the related region label. According to the volume of areas A1, STG, SPG, and V1, they have 1, 11, 13, and 11 parcels, respectively. Therefore in total 36 parcels from 4 areas assigned as AVIN nodes from the total of 954 ROIs. It is essential to indicate the relationships between nodes to make network [43]. Thus, we used Pearson's correlation coefficients to indicate the functional relation between the performances of nodes [44]. Coefficients are between -1 and 1, which can show the direction and strength of connectivity between two nodes. We just used absolute values of coefficients to make undirected weighted networks. Next, we calculated the adjacency matrix for each participant by zeroing the elements on the main diagonal of the absolute coefficients matrix.

2.3. Bootstrap

We divided the whole developmental age range into smaller intervals to analyze the changes in AVIN better. According to the age distribution of participants, we have shorter intervals in the early stages when the rate of developmental change is faster. The selected age ranges and the number of samples per interval are shown in Figure 1B.

We used the statistical method of bootstrap to compare different groups with non-uniformly distribution samples. The process was as follows:

a) First, we selected ten samples from each temporal bin using the sampling with replacement method.
b) Then we calculated the average adjacency matrix by the adjacency matrix of the selected samples.
c) We repeated steps a and b 1000 times to obtain the bootstrap distribution for each range (Figure 1C).
d) The averaged network of each group was computed using the mean of the obtained bootstrap distribution (Figure 1D) [31].

The averaged networks had different densities, so we extracted Maximum Spanning Tree (MST) from each network to make them comparable.

2.4. The Maximum Spanning Tree

MST is a sub-network that connects all network nodes without creating a loop consisting of links that make the total links weight maximum possible. It is unique for brain networks because of the distinct weights while retaining the dynamics and features of the main network. We used improved Kruskal's algorithm to find MSTs [45]. We calculated the MST for each averaged network in all intervals. Then we extracted the measures of each MST to inquire differences through intervals. The definition and calculation methods of MST measures used are summarized in Table 2.

2.5. Multi-scale temporal network

The MST of each group indicates AVIN activity in the relevant interval that changes with growth. We made two types of multi-scale networks to represent the changes made in AVIN better. The constructed network had the same nodes as MSTs but to make links, we had two different scenarios:

A) In the first scenarios, we determined links as follow rules:

- The link weight will be one if there is a link between tantamount pairs of nodes in at least one MST.
- The link weight will be two if its equivalent links exist in all MSTs.

Therefore, the resulting network has two types of links: (1) The stationary links during development that retained their value and importance in network; (2) Links that have been removed or added which their importance has changed over time in AVIN.

B) In another scenario, we omitted fixed links across MSTs to make the second multi-scale network and bring to light the made changes over time. Then we redrew links using color coding to emphasize their creation time in various MSTs.

2.6. Intraregional and interregional links

Each brain region plays a role in separate functions. So it can be beneficial to explore the relation of the changes in links between areas. Hence, we named the links between nodes in the same region as intraregional links and the links between nodes in two separate regions as interregional links to highlight kinds of changes. Then we obtained the percentage of changes in these two types of links. To represent the rate of the change better, we calculated total changes, which are the sum of the interregional and intraregional links changes. Also, we computed the cumulate sum of total changes. The amount of change can show how fast the network modifies over time. Further, we named the ratio of interregional to intraregional links by the measure *R* (Relation 1):

$$R = \frac{Interregional\ links}{Intraregional\ links} \quad (1)$$

R changes can be a good criterion to study alterations in the relationship between involved areas in the AVI process.

3. Results

The main objective of this research was to study AVIN changes during development. We used the preprocessed ADHD200 dataset. We only used the data of TD individuals, who were in the age range of 7 to 14 years. We omitted the results of the 14-22 year group due to the nonuniform distribution (mean: 17.065, STD: 3.407). We divided the age range into smaller intervals to examine the changes in the network so that there are at least eight samples in each age range (Figure 1B). We created 1000 networks from the data of individuals in each interval based on the bootstrap method (Figure 1C). Then we calculated the average network for each group (Figure 1D). In the next step, we extracted the relevant MST of each averaged network and obtained the measures of each MST (Figure 2).

3.1. Analysis of MSTs' measures

In exploring MST measures, we obtained diameter, path length, and leaf fraction. We face two increases in the ages of 7/6 to 8/0 years and 9/9 years in diameter (Figure 2A) and path length (Figure 2B) quantities over time which decreases again by passing these ages. In addition, a slight increase is seen in these two graphs in 9/0 years.

In Figure 2C, we see the fluctuations of the leaf fraction diagram in the early age groups are minor meanwhile, it increases with growth. It can be said that in early intervals most changes occur in inner links, not in leaves. However, we see alterations raises and more variations occur in later intervals. The overlap plot (Figure 2D) shows major changes between subsequent MSTs. The overlap plot shows higher differences between the MSTs in 8/0 to 10/0 years. These variations are severe at 8/3 and between 9/3 to 9/9 years, then overlap increases to reach its maximum value at 11/0, and then decreases slightly.

3.2. Development in MSTs

As we mentioned in the method section, the multi-scale network was obtained from the data. This presentation characterizes the changes in MSTs better in different age ranges. As shown in Figure 3A, links that have retained their importance during development are generally related to intraregional links. The link between the A1 and STG is the only remaining interregional link. It is noteworthy that the A1 node has the maximum degree among all nodes, which shows its importance in the network. In addition, V1 has the highest degree after A1. High-degree nodes in the network are known as hub points of the network. We see that these nodes have reserved their importance in the network during developmental changes in links based on Figure 3B. However, this is entirely different for the S2 node, and its 3 degrees is related to constant links. Afterward, S2 loses its importance during development. Removing constant links does not impact the nodes of the SPG region, and they preserve their importance in relation to other nodes in SPG.

In comparing constant links with altered links, interregional links have a higher proportion of changes. It demonstrates the exchange of the importance of links over time and shows how different links get higher ranks. Exploring temporal changes in links in Figure 3B indicate changes in different development stages. The network tolerates the bulk of changes in the early stages. SPG region has the maximum changes in the initial intervals, and STG links change more at endpoints. Links of V1 and A1 change through the whole developmental process.

3.3. Changes in dynamics of interregional and intraregional links

We explored the dynamics of the interregional and intraregional links to show the rate of changes during development in Figure 4A. In addition, we examined the sum of the changes and their cumulative sum. According to the results, the highest rate of changes is in early intervals; then, it decreases over time. Intraregional links show more changes in the early stages, whereas interregional links show a relatively constant rate of changes. The *R* ratio of interregional links changes is shown in Figure 4B. We see that the pattern of *R* is increasing despite its fluctuation. This means that some intraregional links in MSTs are replaced by interregional links, and intermediary links become more important in the AVIN structure.

4. Discussion

In this work, we explored the changes in AVIN during development. Most fMRI studies in the field of AVI have focused on examining the activity of involved areas while performing AV tasks. They showed that in the early stages of the AV stimulus processing A1, V1, STG, and SPG [19,23] areas display higher activities (Figure 1A). However, the connections between areas have not been studied well. While researchers have shown that the function of AVI depends on the relationship of the involved areas and the dynamics of the interaction between them [26]. Therefore, we used the network approach to study the areas involved in AVI. Using the network approach provides a holistic perspective to scrutinize phenomena, and its results have high generalizability [46]. Accordingly, in addition to examining the activity of the areas, we were able to characterize the relationship between them and the changes taking place during development. Moreover, MST method is reported as a proper tool in brain network studies, which makes unbiased comparisons between networks of individuals in different age groups [34,45]. Notably, using different tasks in studies sometimes lead to results discrepancy in fMRI experiments [47]. We used rs-fMRI data recorded in the open eyes condition. In this case, the results are dependent on the activity of the whole network and are independent of the task used in task-based studies.

4.1. Critical ages in AVIN development

The effects of multisensory integration appear in the performance of individuals after the age of 7, and by getting older, its accuracy goes closer to the performance of adults [15]. Eight years old is the youngest age in which signs of AVI existence have been reported, but it is ambiguous when and how it started. This is due to the broad age range of subjects and different used methods [12,13]. Mathematical models showed the performance of 8 years old subjects tends to benefit from AVI instead of the strategy of switching between modalities [14], but it is not yet clear how this process of changing occurs. So, we used a dataset that have a larger number of participants in the previously studied age ranges. The higher number of samples in the desired age range caused time intervals to be shorter and the results to be more accurate. For each age range, we obtained the average network (Figure 1B-D). Subsequently, we compared MSTs' measures from each averaged network. For the diameter and path length, there are two local peaks in 8 and 9/9 ages (Figure 2A, B). These higher values indicate lower data transferring speeds. The changes in inner branches make these reductions in information flow reach the optimal state because there are not many changes in leaf fraction in the early stages (Figure 2C). Whereas, after 9/9, we see changes in outer links raise as leaf fraction increases. This indicates that the network has reached a stable state, and minor changes are taking place to obtain the optimal state. Changes in overlap (Figure 2D) also show the most remarkable changes at the ages of 8 to 10 years, after which the overlap decreases due to leaf changes. Changes in overlap and leaf fraction show the inner links connected to higher degree nodes, develop first and, then other outer links and leaves will develop.

The overlap raises after ten years old when the function of AVI in temporal tasks goes more similar to adults' one [14,15], but it is still not mature [24]. Showing distorted audio and visual stimuli with different levels of noise revealed that with increasing age from 8 to 10 years, children start benefiting from the advantages of the AVI and gradually improve this ability [6]. Also, researchers reported adult-like high-precision performance in *simultaneity judgment tasks* at the age of 9 [12]. Our results suggest that it can be the impact of the formation or strengthening of network links in the parietal region, which has improved participants' performance (see Figure 3B). Figure 3B represents that most of the link changes in these ages are related to SPG, which plays a role in multisensory spatial localization [22,48], especially in tasks with incongruent AV stimuli [23].

In later age intervals, more changes in the intraregional STG links were observed. Studies have shown that, after age 10, individuals' performance in temporal processing of non-speech AV stimuli increases [24]. Likewise, fMRI studies confirm increasing STG activity during doing these tasks [23,25]. Eventually, improving intraregional communication in STG can bring performance closer to adults. As getting older, the activity of STG decreases during the task (compared to younger children) [25]; it is the sign of reaching the optimal AVI state. Consequently, changes in STG are the final step in the development of AVIN.

4.2. Rate of changes in AVIN links

During development, some links remain fixed between trees (red links in Figure 3A). We hypothesized that these links establish the basic connections to perform the main function of areas. Meanwhile, other links change over time (blue links in Figure 3A). During development, children learn to benefit from the advantages of AVI in the face of AV stimuli [10,12,14,26,49]. So we propose that blue links play essential roles in AVIN formation. We did not see many changes in the degree of the nodes and the order of their importance after removing the fixed links (Figure 3B); that shows specific nodes have more significant impacts on AVIN performance. This means some subregions in each area play a more important role in the AVI process. Most links changes occur before the age of 9/9, after which there is a noticeable decrease in the slope of the cumulative sum of changes (see purple dashed line in Figure 4A). The high volume of links changes in the early age ranges is a sign of the formation of the main AVIN framework, which causes revelation of the symptoms of benefiting from AVI. This is why previous studies have declared the beginning of AVI at these ages [13–15]. The next volume of changes and decreasing amount of changes can be related to network reconfiguration to improve performance [6,25,50,51].

Links changes between A1 and V1 during development (Figure 3B) indicate that AVIN preserves the value of the interaction between these regions.

The slight increase in the value of *R* (the ratio of intraregional-to-interregional links) in Figure 4B and the new connections made at higher age intervals (Figure 3B) are consistent with the accepted development pattern, which assumes distal strengthening and local weakening in structural and functional connectivity [52]. Variations in the *R* ratio (Figure 4B) and the volume of changes in links (Figure 4A) in the early stages also re-emphasize the importance of the links and AVIN establishment in the early stages.

From a network studies perspective, is our study consistent with other studies conducted on brain networks? A rich-club phenomenon is the interconnection of high-degree nodes with other rich nodes. Studies have shown that in the brain network of adults, there is a higher functional rich-club organization compared to the younger population [53]. Our study shows the strengthening of interregional links and increasing the degree of the corresponding node in older age ranges, which can be consistent with the formation of rich-clubs in the brain. Also, studies have shown connections of the existing brain subnetworks refines from adolescence to early adulthood [54]. Where we observed reducing changes in intermediate link weights and increasing in MST leaves changes. Researchers suggest that these changes cause the development of sensory and cognitive functions [54].

Considering the superior spatial resolution of the fMRI technique, it appears to be a more favorable option for studies like ours, where changes in the connections between different brain regions are of importance. On the other hand, when a higher temporal resolution is required, studies have utilized electroencephalography (EEG) to construct brain networks. Taskov and Dushanova studied changes in brain connectivity before and after visual training using EEG data [55]. Similarly, Fraga-González et al. created and compared the brain networks of individuals during task blocks [56]. Also, using EEG data, researchers have been able to demonstrate the effect of visual training on dyslexia by utilizing the tools of graph theory and MST [55,57]. These studies indicate that graph theory and MST tools can effectively reflect changes in brain networks despite the variation of the neuroimaging techniques used and subjects' conditions.

Finally, we hypothesized that at the first step brain learns to detect the source of the AV stimuli. In this process, the brain examines the spatial location and congruency of AV stimuli. Next, the brain adjusts the timing window that shows received auditory and visual stimuli have been released from the same source if the delay time is in the range of the timing window. As a result, enhancement or rehabilitation programs that want to improve AVI, should include localization tasks before the age of 9/9 and temporal judgment tasks before the age of 11 to accelerate this process.

4.3. Study Limitations

According to our used method, there are some limitations in interpreting the results. We used a rs_fMRI dataset to explore AVIN characteristics independent of AV tasks. In this case, there are slight differences in the performance and the boundaries of the areas. Whereas, researchers showed these studies can provide a reliable method in exploring developmental progress and assessing brain networks in children [44,58]. We used the values of the functional connectivities between the parcels (network nodes) as a criterion to assign links between them. During development, by changing the weight of links some links add to or remove from the MSTs. These changes indicate that the importance of the related connection has increased or decreased. Nevertheless, we cannot determine whether the communication value of the route has altered or a new route has been created between two parcels, or an old route has been demolished. In interpreting the results, it is beneficial to consider whether the structural connections between brain regions change or not [59]. While Researchers in some tractology studies have been found direct connections between A1 and V1 [60,61] and indirect one between STG and SPG [25,61], yet its developmental alterations are unrevealed. Tractological studies are recommended to study developmental changes in the pathways related to AVI. Studies like this will help us clarify the nature of the changes made better.

We extracted MSTs from AVIN to attain comparable networks with the same size and densities. Studies have shown using MST instead of the whole network preserves the main features and dynamics of the main network [34]. Meanwhile, other methods can be used to compare the results of the removing links.

According to the results, a similar study can be repeated on individuals with impaired sensory integration function to figure out abnormal developmental patterns. According to studies on brain plasticity, training affects the process of the AVI and improves the function of the related areas [62,63]. Our findings make it possible to design more effective rehabilitation programs based on critical age ranges to reduce probable time lags or dysfunctions in the AVI process. Also, brain stimulation methods can be performed to strengthen interrelationships between involved areas [64–66].

5. Conclusion

In this study, we scrutinized how AVIN changes during development. We found that AVIN formation takes place gradually and improves over the years. In this process, the spatial localization sub-network is created and evolves in the parietal lobe at first, and at the same time, with a slight delay, the temporal judgment sub-network begins to form and develop in the temporal lobe. Consequently, studies based on different task designs may differ in reporting the age at which individuals start to benefit from AVI.

The highest rate of change occurs in the early stages of development and before the age of 9/9 (years/months). Afterward, the speed of change slows down but does not stop, which is the sign of the network evolution. It is recommended to perform localization tasks for rehabilitation or enhancement of the AVI process in the early stages of development. In the next step, temporal judgment tasks are a good choice to improve children's performance.

Acknowledgements

This work was supported by the Cognitive Sciences and Technologies Council (Grant No. 9875). The authors acknowledge the ADHD-200 Consortium for sharing their recorded data publicly. This study would not have been possible without using this dataset.

Data availability

The dataset analysed during the current study is publicly available in the Neuroimaging Informatics Tools and Resources Collaboratory (NITRC) repository, [http://neurobureau.projects.nitrc.org/ADHD200/Introduction.html; RRID:SCR_000576].

Statements and Declarations

Funding

This work was supported by the Cognitive Sciences and Technologies Council (Grant Number 9875).

Competing Interests

The authors have no relevant financial or non-financial interests to disclose.

Author Contributions

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Abbas Pourhedayat, Fatemeh Bakouie and Shahriar Gharibzadeh. The first draft of the manuscript was written by Abbas Pourhedayat and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

References

1. Gao, C., Green, J. J., Yang, X., et al., "Audiovisual integration in the human brain: a coordinate-based meta-analysis", *Cereb. Cortex*, **33**(9), pp. 5574–5584 (2023).

2. Tye-Mmurray, N., Spehar, B., Myerson, J., et al., "Lipreading and audiovisual speech recognition across the adult lifespan: Implications for audiovisual integration", *Psychol. Aging*, **31**(4), pp. 380–389 (2016).

3. Pulliam, G., Feldman, J. I., and Woynaroski, T. G., "Audiovisual multisensory integration in individuals with reading and language impairments: A systematic review and meta-analysis", *Neurosci. Biobehav. Rev.*, **149**, p. 105130 (2023).

4. Freeman, L. C. A., Wood, K. C., and Bizley, J. K., "Multisensory stimuli improve relative localisation judgments compared to unisensory auditory or visual stimuli", *J. Acoust. Soc. Am.*, **143**(6), pp. EL516–EL522 (2018).

5. Odegaard, B., Beierholm, U. R., Carpenter, J., et al., "Prior expectation of objects in space is dependent on the direction of gaze", *Cognition*, **182**, pp. 220–226 (2019).

6. Barutchu, A., Danaher, J., Crewther, S. G., et al., "Audiovisual integration in noise by children and adults", *J. Exp. Child Psychol.*, **105**(1), pp. 38–50 (2010).

7. Feldman, J. I., Dunham, K., Cassidy, M., et al., "Audiovisual multisensory integration in individuals with autism spectrum disorder: A systematic review and meta-analysis", *Neurosci. Biobehav. Rev.*, **95**, pp. 220–234 (2018).

8. Stevenson, R. A., Segers, M., Ferber, S., et al., "Keeping time in the brain: Autism spectrum disorder and audiovisual temporal processing", *Autism Res.*, **9**(7), pp. 720–738 (2016).

9. Ronconi, L., Vitale, A., Federici, A., et al., "Neural dynamics driving audio-visual integration in autism", *Cereb. Cortex*, **33**(3), pp. 543–556 (2023).

10. Taylor, N., Isaac, C., and Milne, E., “A Comparison of the Development of Audiovisual Integration in Children with Autism Spectrum Disorders and Typically Developing Children”, *J. Autism Dev. Disord.*, **40**(11), pp. 1403–1411 (2010).

11. Dionne-Dostie, E., Paquette, N., Lassonde, M., et al., “Multisensory Integration and Child Neurodevelopment”, *Brain Sci.*, **5**(1), pp. 32–57 (2015).

12. Chen, Y.-C., Shore, D. I., Lewis, T. L., et al., “The development of the perception of audiovisual simultaneity”, *J. Exp. Child Psychol.*, **146**, pp. 17–33 (2016).

13. Hillock-Dunn, A. and Wallace, M. T., “Developmental changes in the multisensory temporal binding window persist into adolescence”, *Dev. Sci.*, **15**(5), pp. 688–696 (2012).

14. Adams, W. J., “The Development of Audio-Visual Integration for Temporal Judgements”, *PLOS Comput. Biol.*, **12**(4), p. e1004865 (2016).

15. Kaganovich, N., “Development of sensitivity to audiovisual temporal asynchrony during midchildhood”, *Dev. Psychol.*, **52**(2), pp. 232–241 (2016).

16. Kaganovich, N. and Schumaker, J., “Audiovisual integration for speech during mid-childhood: Electrophysiological evidence”, *Brain Lang.*, **139**, pp. 36–48 (2014).

17. Vannasing, P., Dionne-Dostie, E., Tremblay, J., et al., “Electrophysiological responses of audiovisual integration from infancy to adulthood”, *Authorea Prepr.* (2023).

18. Doehrmann, O. and Naumer, M. J., “Semantics and the multisensory brain: How meaning modulates processes of audio-visual integration”, *Brain Res.*, **1242**, pp. 136–150 (2008).

19. Koelewijn, T., Bronkhorst, A., and Theeuwes, J., “Attention and the multiple stages of multisensory integration: A review of audiovisual studies”, *Acta Psychol. (Amst).*, **134**(3), pp. 372–384 (2010).

20. Brang, D., Taich, Z. J., Hillyard, S. A., et al., “Parietal connectivity mediates multisensory facilitation”, *Neuroimage*, **78**, pp. 396–401 (2013).

21. Calvert, G. A., Hansen, P. C., Iversen, S. D., et al., “Detection of audio-visual integration sites in humans by application of electrophysiological criteria to the BOLD effect.”, *Neuroimage*, **14**(2), pp. 427–438 (2001).

22. Molholm, S., Sehatpour, P., Mehta, A. D., et al., “Audio-Visual Multisensory Integration in Superior Parietal Lobule Revealed by Human Intracranial Recordings”, *J. Neurophysiol.*, **96**(2), pp. 721–729 (2006).

23. Fitzhugh, M. C., Whitehead, P. S., Johnson, L., et al., “A functional MRI investigation of crossmodal interference in an audiovisual Stroop task”, *PLoS One*, **14**(1), p. e0210736 (2019).

24. Murray, M. M. and Wallace, M. T., “The neural bases of multisensory processes”, *Neural Bases Multisensory Process.*, pp. 1–757 (2011).

25. Powers, A. R., Hevey, M. A., and Wallace, M. T., “Neural correlates of multisensory perceptual learning”, *J. Neurosci.*, **32**(18), pp. 6263–6274 (2012).

26. Dick, A. S., Solodkin, A., and Small, S. L., “Neural development of networks for audiovisual speech comprehension”, *Brain Lang.*, **114**(2), pp. 101–114 (2010).

27. Puxeddu, M. G., Faskowitz, J., Sporns, O., et al., “Multi-modal and multi-subject modular organization of human brain networks”, *Neuroimage*, **264**, p. 119673 (2022).

28. Nigro, S., Filardi, M., Tafuri, B., et al., “The Role of Graph Theory in Evaluating Brain Network Alterations in Frontotemporal Dementia”, *Front. Neurol.*, **13**, p. 910054 (2022).

29. Liu, M., Amey, R. C., Backer, R. A., et al., “Behavioral Studies Using Large-Scale Brain Networks – Methods and Validations”, *Front. Hum. Neurosci.*, **16**, p. 875201 (2022).

30. Barabási, D. L., Bianconi, G., Bullmore, E., et al., “Neuroscience Needs Network Science”, *J. Neurosci.*, **43**(34), pp. 5989–5995 (2023).

31. Puxeddu, M. G., Faskowitz, J., Betzel, R. F., et al., “The modular organization of brain cortical connectivity across the human lifespan”, *Neuroimage*, **218**, p. 116974 (2020).

32. van Wijk, B. C. M., Stam, C. J., and Daffertshofer, A., “Comparing Brain Networks of Different Size and Connectivity Density Using Graph Theory”, *PLoS One*, **5**(10), p. e13701 (2010).

33. Blomsma, N., Rooy, B., Gerritse, F., et al., “Minimum spanning tree analysis of brain networks: A systematic review of network size effects, sensitivity for neuropsychiatric pathology, and disorder specificity”, *Netw. Neurosci.*, **6**(2), pp. 301–319 (2022).

34. Tewarie, P., van Dellen, E., Hillebrand, A., et al., “The minimum spanning tree: An unbiased method for brain network analysis”, *Neuroimage*, **104**, pp. 177–188 (2015).

35. Kruskal, J. B., “On the Shortest Spanning Subtree of a Graph and the Traveling Salesman Problem”, *Proc. Am. Math. Soc.*, **7**(1), p. 48 (1956).

36. Požar, R., Kero, K., Martin, T., et al., “Task aftereffect reorganization of resting state functional brain networks in healthy aging and mild cognitive impairment”, *Front. Aging Neurosci.*, **14**, p. 1061254 (2023).

37. Jia, H., Wu, X., Wu, Z., et al., “Aberrant dynamic minimal spanning tree parameters within default mode network in patients with autism spectrum disorder”, *Front. Psychiatry*, **13**, p. 860348 (2022).

38. Canario, E., Chen, D., Han, Y., et al., “Global Network Analysis of Alzheimer’s Disease with Minimum Spanning Trees”, *J. Alzheimer’s Dis.*, **89**(2), pp. 571–581 (2022).

39. ADHD200 Consortium, “The ADHD-200 Consortium: a model to advance the translational potential of neuroimaging in clinical neuroscience”, *Front. Syst. Neurosci.*, **6**(SEPTEMBER), pp. 1–5 (2012).

40. Lavoie-Courchesne, S., Rioux, P., Chouinard-Decorte, F., et al., “Integration of a neuroimaging processing pipeline into a pan-canadian computing grid”, *J. Phys. Conf. Ser.*, Institute of Physics Publishing, p. 012032 (2012).

41. Bellec, P., Chu, C., Chouinard-Decorte, F., et al., “The Neuro Bureau ADHD-200 Preprocessed repository”, *Neuroimage*, **144**, pp. 275–286 (2017).

42. Rolls, E. T., Huang, C. C., Lin, C. P., et al., “Automated anatomical labelling atlas 3”, *Neuroimage*, **206**, p. 116189 (2020).

43. Rubinov, M. and Sporns, O., “Complex network measures of brain connectivity: Uses and interpretations”, *Neuroimage*, **52**(3), pp. 1059–1069 (2010).

44. Thomason, M. E., Dennis, E. L., Joshi, A. A., et al., “Resting-state fMRI can reliably map neural networks in children”, *Neuroimage*, **55**(1), pp. 165–175 (2011).

45. Stam, C. J., Tewarie, P., Van Dellen, E., et al., “The trees and the forest: Characterization of complex brain networks with minimum spanning trees”, *Int. J. Psychophysiol.*, **92**(3), pp. 129–138 (2014).

46. Braun, U., Schaefer, A., Betzel, R. F., et al., “From Maps to Multi-dimensional Network Mechanisms of Mental Disorders”, *Neuron*, **97**(1), pp. 14–31 (2018).

47. Callan, D. E., Jones, J. A., Munhall, K., et al., “Neural processes underlying perceptual enhancement by visual speech gestures”, *Neuroreport*, **14**(17) (2003).

48. Rohe, T. and Noppeney, U., “Distinct Computational Principles Govern Multisensory Integration in Primary Sensory and Association Cortices.”, *Curr. Biol.*, **26**(4), pp. 509–14 (2016).

49. Tremblay, C., Champoux, F., Voss, P., et al., “Speech and Non-Speech Audio-Visual Illusions: A Developmental Study”, *PLoS One*, **2**(8), p. e742 (2007).

50. Mukai, I., Kim, D., Fukunaga, M., et al., "Activations in Visual and Attention-Related Areas Predict and Correlate with the Degree of Perceptual Learning", *J. Neurosci.*, **27**(42), pp. 11401–11411 (2007).

51. Hillock, A. R., Powers, A. R., and Wallace, M. T., "Binding of sights and sounds: Age-related changes in multisensory temporal processing", *Neuropsychologia*, **49**(3), pp. 461–467 (2011).

52. Boersma, M., Smit, D. J. a., Boomsma, D. I., et al., "Growing Trees in Child Brains: Graph Theoretical Analysis of Electroencephalography-Derived Minimum Spanning Tree in 5- and 7-Year-Old Children Reflects Brain Maturation", *Brain Connect.*, **3**(1), pp. 50–60 (2013).

53. Kim, D. J. and Min, B. K., "Rich-club in the brain's macrostructure: Insights from graph theoretical analysis", *Comput. Struct. Biotechnol. J.*, **18**, pp. 1761–1773 (2020).

54. Edde, M., Leroux, G., Altena, E., et al., "Functional brain connectivity changes across the human life span: From fetal development to old age", *J. Neurosci. Res.*, **99**(1), pp. 236–262 (2021).

55. Taskov, T. and Dushanova, J., "Reading-Network in Developmental Dyslexia before and after Visual Training", *Symmetry (Basel).*, **12**(11), p. 1842 (2020).

56. Fraga-González, G., Smit, D. J. A., Van der Molen, M. J. W., et al., "Graph Analysis of EEG Functional Connectivity Networks During a Letter-Speech Sound Binding Task in Adult Dyslexics", *Front. Psychol.*, **12**, p. 767839 (2021).

57. Xue, H., Wang, Z., Tan, Y., et al., "Resting-state EEG reveals global network deficiency in dyslexic children", *Neuropsychologia*, **138**, p. 107343 (2020).

58. Rosazza, C. and Minati, L., "Resting-state brain networks: Literature review and clinical applications", *Neurol. Sci.*, **32**(5), pp. 773–785 (2011).

59. van den Heuvel, M. P. and Hulshoff Pol, H. E., "Exploring the brain network: A review on resting-state fMRI functional connectivity", *Eur. Neuropsychopharmacol.*, **20**(8), pp. 519–534 (2010).

60. Beer, A. L., Plank, T., and Greenlee, M. W., “Diffusion tensor imaging shows white matter tracts between human auditory and visual cortex”, *Exp. Brain Res.*, **213**(2–3), pp. 299–308 (2011).

61. Brang, D., Taich, Z. J., Hillyard, S. A., et al., “Parietal connectivity mediates multisensory facilitation”, *Neuroimage*, **78**, pp. 396–401 (2013).

62. Paraskevopoulos, E. and Herholz, S., “Multisensory integration and neuroplasticity in the human cerebral cortex”, *Transl. Neurosci.*, **4**(3), pp. 337–348 (n.d.).

63. Ihalainen, R., Kotsaridis, G., Vivas, A. B., et al., “The relationship between musical training and the processing of audiovisual correspondences: Evidence from a reaction time task”, *PLoS One*, **18**(4), p. e0282691 (2023).

64. Tseng, P., Iu, K. C., and Juan, C. H., “The critical role of phase difference in theta oscillation between bilateral parietal cortices for visuospatial working memory”, *Sci. Rep.*, **8**(1), pp. 1–9 (2018).

65. Reinhart, R. M. G. and Nguyen, J. A., “Working memory revived in older adults by synchronizing rhythmic brain circuits”, *Nat. Neurosci.*, **22**(5), pp. 820–827 (2019).

66. Pei, C., Qiu, Y., Li, F., et al., “The different brain areas occupied for integrating information of hierarchical linguistic units: a study based on EEG and TMS”, *Cereb. Cortex*, **33**(8), pp. 4740–4751 (2023).

Abbas Pourhedayat is a PhD candidate in Cognitive modeling at the Institute for Cognitive and Brain Sciences (ICBS) of Shahid Beheshti University, Tehran, Iran. He received his MSc in Biomedical Engineering from Iran University of Science & Technology. His research interest includes visual neuroscience and neurodevelopmental disorders, and his current research focuses on developmental models of multisensory integration.

Shahriar Gharibzadeh is an Associate Professor at the Institute for Cognitive and Brain Sciences (ICBS), Shahid Beheshti University, Iran. He received his M.D. in 1992 from Tehran University of Medical Sciences, and PhD in physiology in 1998 from Tehran University. He is interested in theoretical studies and modeling in neuroscience and neurophilosophy.

Fatemeh Bakouie is an Assistant Professor at the Institute for Cognitive and Brain Sciences (ICBS), Shahid Beheshti University, Iran. She received her PhD degree in Biomedical Engineering (Bioelectric) Faculty of Biomedical Engineering, Amirkabir University of Tehran (Tehran Polytechnique) in 2012. Her current research focuses on Network Science and its applications in Brain and Cognitive Science.

Table Captions

Table 1: Regions of interest within the left hemisphere that were used to make the audiovisual integration network (AVIN).

Table 2: Explanation of the maximum spanning tree (MST)'s measures.

Figure Captions

Figure 1: Steps of audiovisual integration network (AVIN) formation in different age groups

A- The involved brain areas in the audiovisual integration process.

B- The number of participants based on age ranges. The horizontal axis shows the age range in years/months format, and the vertical axis shows the number of samples in each bin.

C- The bootstrap method was used and repeated 1000 times for each age group.

D- The overall network was obtained from mean bootstrapped adjacency matrices.

Figure 2: Diameter (A), path length (B), leaf fraction (C), and normalized value of overlap between two MSTs in a row (D) of the maximum spanning trees (MST) in different age intervals

Figure 3: The multi-scale and equivalent anatomically networks formed from the changed links in MSTs of various age ranges. The size of each node is proportional to its degree.

A- The multi-scale network shows stationary (red) versus varied (blue) links.

B- The changed links by development (the blue links in Figure 3A) are shown according to their age changes with the color coding. The cyan color is related to the lower age ranges.

Figure 4: Showing changes in interregional and intraregional links

A- Chang percentage of intraregional links number (red) to the interregional links (blue), total changes (yellow dashed line), and cumulative sum of changes (violet dashed line)

B- The ratio of interregional links (blue columns in the cyan background) to the total links

Tables

Table 1:

REGION	ANATOMICAL DESCRIPTION	AAL3 LABEL	AAL3 No.
A1	Heschl’s gyrus	Heschl_L	83
STG	Superior temporal gyrus	Temporal_Sup_L	85
SPG	Superior parietal gyrus	Parietal_Sup_L	63
V1	Calcarine fissure and surrounding cortex	Calcarine_L	47

MEASURE	EXPLANATION	FORMULA
SHORTEST PATH	The fewest links between two nodes of an MST	
DIAMETER	The longest shortest path in the MST (normalized by network size)	$D = \frac{d}{M}$
PATH LENGTH	The average of the shortest paths of a tree	$L_p = \frac{1}{N} \sum_i \frac{\sum_{j, j \neq i} d_{ij}}{1 - N}, i, j \in N$
LEAF FRACTION	The ratio of the number of nodes with first degree to the total number of links	$L_f = \frac{L}{M}$
OVERLAP	The ratio of shared links between MST_i and MST_j to total links	$O = \frac{MST_i \cap MST_j}{M}$
N	Number of nodes	

Table 2:

M	M is the total number of links
d	The longest shortest path in MST
d_{ij}	The topological distance (the inverse of the link weights) between nodes i and j
L	The number of the nodes with degree one

Figures

Figure 1:

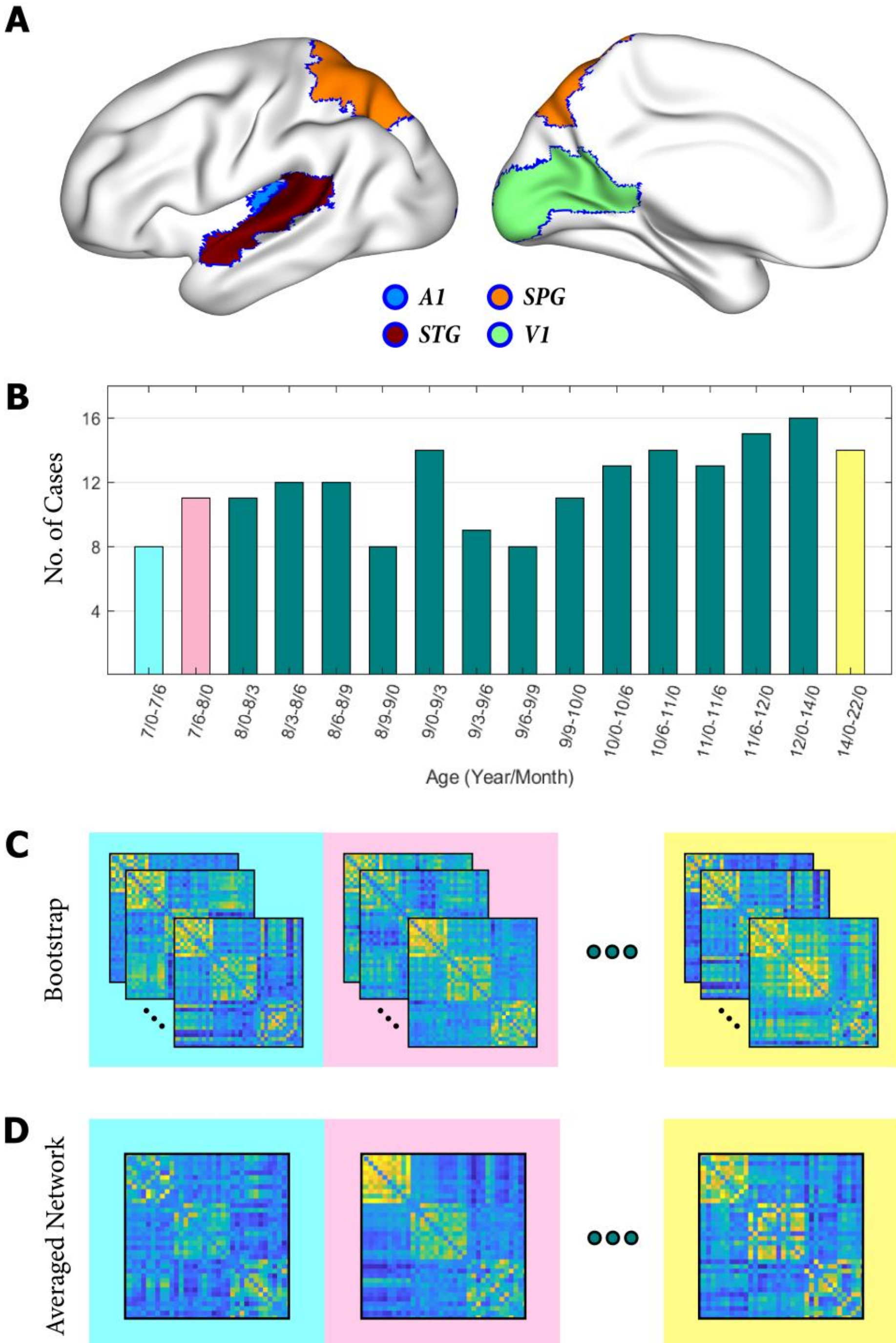
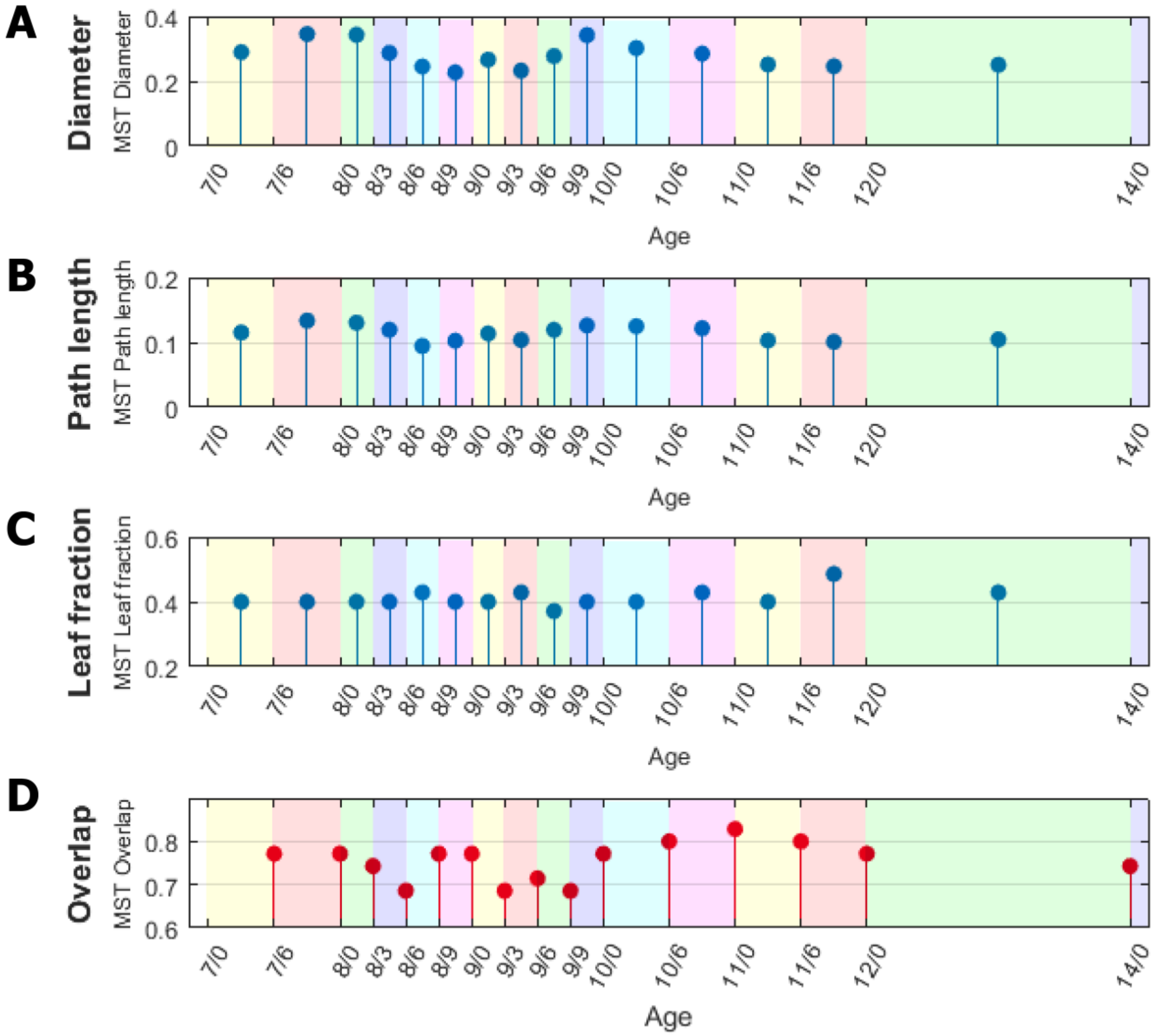


Figure 2:



A
Diameter
MST Diameter
0.4
0.2
0
7/0
7/6
8/0
8/3
8/6
8/9
9/0
9/3
9/6
9/9
10/0
10/6
11/0
11/6
12/0
14/0
Age
B
Path length
MST Path length
0.2
0.1
0
Age
C
Leaf fraction
MST Leaf fraction
0.6
0.4
0.2
Age
D
Overlap
MST Overlap
0.8
0.7
0.6
Age

Figure 3:

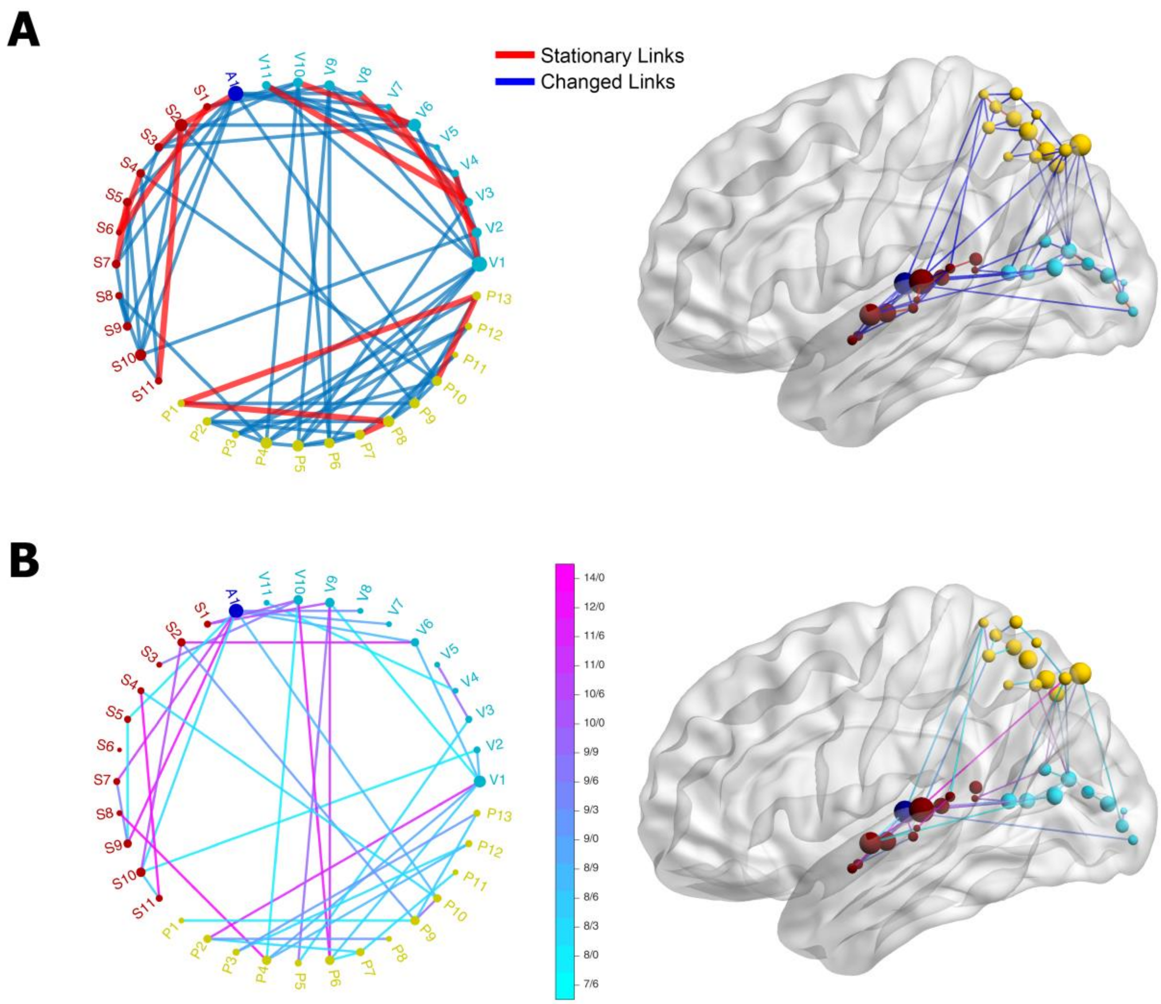
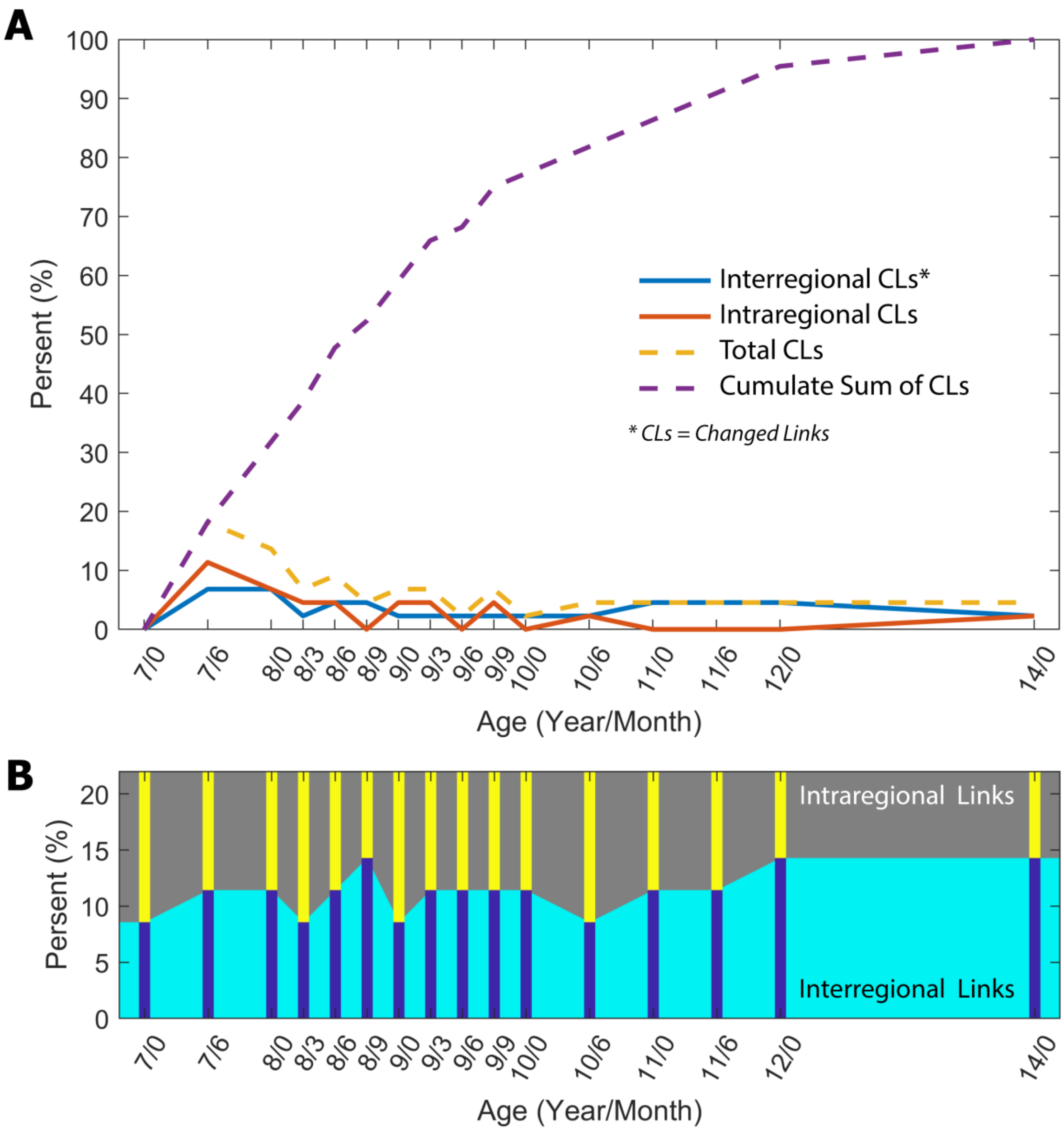

A
Stationary Links
Changed Links
A1
S1
S2
S3
S4
S5
S6
S7
S8
S9
S10
S11
V1
V2
V3
V4
V5
V6
V7
V8
V9
V10
V11
P1
P2
P3
P4
P5
P6
P7
P8
P9
P10
P11
P12
P13
B
14/0
12/0
11/6
11/0
10/6
10/0
9/9
9/6
9/3
9/0
8/9
8/6
8/3
8/0
7/6

Figure 4:


A
B
Persent (%)
Age (Year/Month)
Interregional CLs*
Intraregional CLs
Total CLs
Cumulate Sum of CLs
* CLs = Changed Links
Intraregional Links
Interregional Links
7/0
7/6
8/0
8/3
8/6
8/9
9/0
9/3
9/6
9/9
10/0
10/6
11/0
11/6
12/0
14/0