TSTAI: A Time-varying Brain Effective Connectivity Network Construction Method Combining with Brain Active Information

Qi Chen[1], **Zhiqiong Wang**[1 *], **Jiaxin Li**[2], **Jinying Tao**[2] and **Junchang Xin**[2,3]
[1]College of Medicine and Biological Information Engineering, Northeastern University, Shenyang, China
[2]School of Computer Science And Engineering, Northeastern University, Shenyang, China
[3]Key Laboratory of Big Data Management and Analytics (Liaoning Province), Shenyang, China
2310503@stu.neu.edu.cn, wangzq@bmie.neu.edu.cn, 2201814@stu.neu.edu.cn,
tao13623625013@163.com, xinjunchang@mail.neu.edu.cn

Abstract

More accurate construction of brain effective concetivity networks remains a great challenge to achieve accurate auxiliary diagnosis of brain diseases and in-depth exploration of brain function. However, existing methods only consider higher-order or non-stationary assumptions, rather than simultaneously constructing higher-order and non-stationary networks. Among many existing methods, Bayesian network methods demonstrate superior network structure learning ability. In this work, the forward-backward search (FBS) method is optimized by using brain active information, which is improved to a higher-order network structure learning method, called TSTAI. Firstly, in the process of non-stationary network structure learning, two-stage idea is used to search the change points. Then, in the process of learning higher-order network structure, FBS method is combined with two kinds of brain active information to improve the condition set filtering process and scoring function, respectively. Finally, the pruning strategy is used to reduce the search space. Extensive experiments on simulated and real data demonstrate the effectiveness of TSTAI. Through experiments, the TSTAI is compared with state-of-the-art higher-order network construction methods, and the proposed method achieves an improvement of 3.6% and 17.4% respectively in the network construction accuracy.

1 Introduction

Understanding the complex dynamics of the human brain, as well as its numerous interconnected regions and complex causal relationships, remains one of the most striking challenges in neuroscience [Ji *et al.*, 2021; Shuyue Xu and Liang, 2023a; Qu *et al.*, 2023]. With the continuous development of brain imaging technology, such as fMRI and EEG, it is now possible to observe brain activity non-invasively [Ge *et al.*, 2020; Paolo Maria Rossini and Vecchio, 2022]. Brain network technology has emerged. At present, the research on brain networks is mainly divided into three categories, including structural network, functional network and effective connectivity network [Shuyue Xu and Liang, 2023b; Toshiki Orihara and Tanaka, 2023]. Compared with the other two kinds of networks, edges in effective connectivity networks exhibit directionality [Li *et al.*, 2018; Pervaiz *et al.*, 2020; Liu *et al.*, 2024a]. Besides, it can describe the direction of information flow in the brain interval and contain more information, which makes it highly worthwhile to conduct further research [Ma *et al.*, 2024].

Probabilistic, statistical and graph theory-based Bayesian networks (BNs) provide a promising approach to capture the complexity of brain dynamics [Patel *et al.*, 2006; Du *et al.*, 2019; Xin *et al.*, 2024]. So BN has gradually become one of the important methods to learn directed networks, and is gradually being applied in the process of constructing brain effective connectivity networks [Wang *et al.*, 2024]. However, BN structure learning has always been an NP-hard problem [Saetia *et al.*, 2021; Wang *et al.*, 2025]. Meanwhile, many optimization methods have been proposed in recent years [Li *et al.*, 2015]. In the field of brain science, the active information of the brain has always been the focus of people's exploration [Patel *et al.*, 2006]. The active information of the brain can not only provide rich information for in-depth exploration of brain function, but also act as an auxiliary diagnostic marker for some brain diseases. In 2016 and 2019, Ji *et al* [Junzhong *et al.*, 2016; Liu *et al.*, 2020] developed two swarm intelligence algorithms combining brain activity information to infer effective connectivity from fMRI data. Using two stochastic global search mechanisms in the candidate solution space, both methods achieve higher accuracy in identifying effective connectivity orientation than traditional methods. However, the existing optimization methods only consider the probability statistics calculated from the brain active state that Patel has proposed [Patel *et al.*, 2006], but do not consider the hierarchical structure derived from the active state of brain regions.

Besides, nowadays most of network construction methods need to be based on stationary and first-order Markov assumptions, which is inconsistent with the complex working states of human brain [Tan *et al.*, 2023; Esch *et al.*, 2020]. Moreover, there are very few methods to construct brain effective connectivity networks based on these two assump-

*Corresponding author

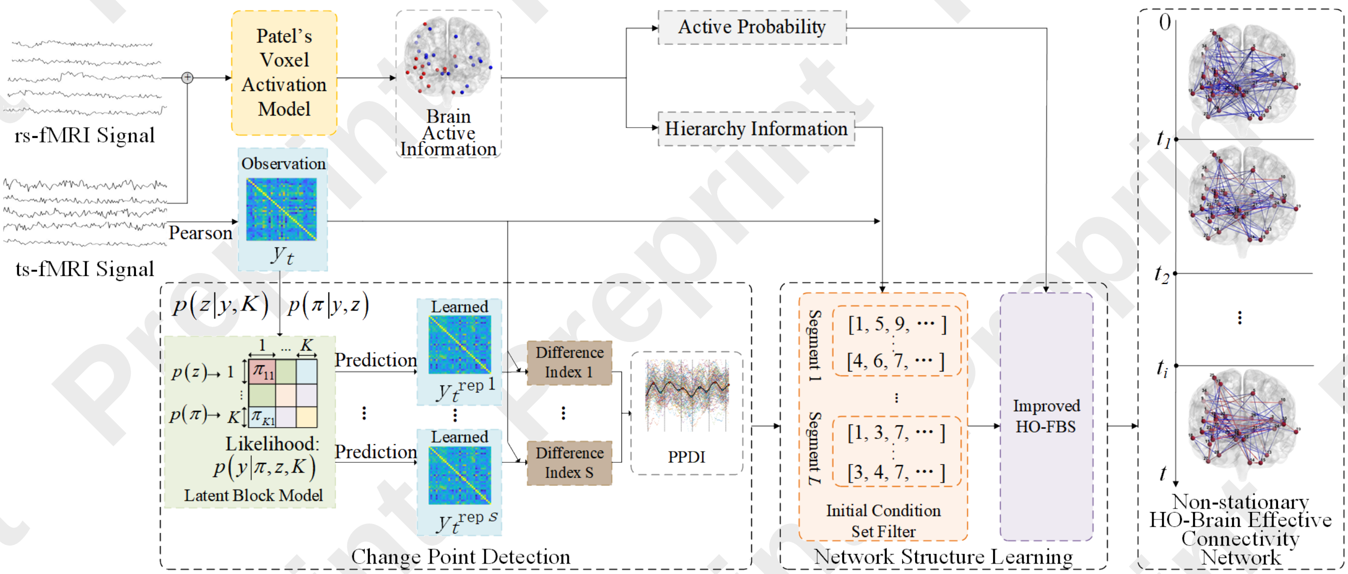


Figure 1: The Framework for TSTAI Method

tions simultaneously. A wealth of research has demonstrated that brain connection patterns are complex and dynamic [Aldarondo *et al.*, 2024; Lynch *et al.*, 2024]. Therefore, it is highly necessary to propose a method for constructing brain effective connectivity networks that can take these two assumptions into account simultaneously. To overcome these limitations, we propose a novel Two-Stage higher order brain effective connectivity network construction method combining with Two kinds of brain Activation Information based on non-stationary time series (TSTAI). Overall, the contributions of this paper can be summarized as:

- A structure learning method of higher-order non-stationary brain effective connectivity network based on fusion of two kinds of brain active information is proposed, called TSTAI.
- In the condition set filtering stage, the search space is reduce using the hierarchical structure of the brain active information. Besides, a pruning strategy is used to reduce the number of candidate networks and improve the search efficiency in each round of the optimal network structure searching.
- A novel scoring function for network structure learning is proposed in combination with active information. It can achieve more precise orientation to fuzzy edges and achieve more accurate brain effective connectivity network construction.

2 Method

In reality, brain is a highly complex system [Bossier *et al.*, 2020; Xu *et al.*, 2016]. So a simplistic first-order assumption falls short in accurately simulating its working states[Yang *et al.*, 2022]. Therefore, we propose a higher-order non-stationary method to construct brain effective connectivity networks. The overall framework is illustrated in Fig. 1. In this part, firstly, the proposed higher order brain effective connectivity network construction method combining with brain activation information based on non-stationary time series is introduced. After that, the active information extraction and higher order network structure learning are introduced in detail. In the part of network structure learning, an improved HO-DBN method combining with brain activation information is prosed to reduce the initial search space and mprove the learning efficiency of network structure.

2.1 Definition

Let X_n denote brain signals from brain region, with $X_n^T = \left(x_n^1, ..., x_n^t, ..., x_n^T\right) \ \ (t = 1, ..., T)$ representing the time series of region n, where T represents the length of time series. And x_n^t represents the fMRI time series value of brain regions n at time t. D represents the time series set observed in all N brain regions. $Pa\left(X_n\right)$ represents the parent node set of X_n.

Let $G =< V, E >$ represents a directed network, in which V represents the node set in the network, that is, the brain regions of interest selected for the construction of the brain effective connectivity network. E represents the directed edge set in the network, which represents the influence relationship between one brain region and another brain region in the brain effective connectivity network. $e_{i,j}$ exist if and only if there is effective connectivity between brain regions. Scoring function J is used to quantitatively evaluate the quality of fitting degree between candidate networks G and data D, which is expressed as $J\left(G\,|D\right)$. Usually, inferring a brain effective connectivity network from fMRI data can be regarded as searching a network G that can best fit the data D according to the scoring function.

2.2 Two-Stage Higher Order Brain Effective Connectivity Network Construction Method

In recent years, research has shown that the connection pattern of the brain is more complex in the task state, and brain states dynamically change during different tasks. Therefore, the traditional brain effective connectivity network construction method based on the assumption of stationary time series is no longer applicable. With the deepening of research, some studies have applied the non-stationary network construction method to the process of brain network construction. However, these methods are all based on the first-order Markov assumption, that is, it is assumed that the state of the brain region at time T is only related to the state at time $T - 1$ and has nothing to do with other times. In fact, the brain is a system with a very complex working mechanism, and a simple first-order assumption is not sufficient to accurately simulate the working state of the brain. Therefore, we propose a higher-order non-stationary brain effective connectivity network construction method.

The active state of brain regions has always been a focal point in neuroscience, offering abundant information for understanding and analyzing brain function [Bolton *et al.*, 2020]. Patel et al. [Patel *et al.*, 2006] were the first to systematically introduce the concept of brain region activity, proposing two key notions: active probabilistic statistics and the hierarchical structure. In recent years, some studies have applied probabilistic statistics to optimize network structure learning [Junzhong *et al.*, 2016; Akkurt *et al.*, 2023]. Nevertheless, they tend to overlook the crucial concept of hierarchical structure. Hence, we introduce a novel method called TSTAI that integrates two kinds of information into a higher-order brain effective connectivity network structure learning approach, thereby enhancing existing structural learning methods.

The proposed method continues the idea of previous work and conducts the detection of change points and the learning of network structures in two steps. In the part of change point detection, the latent block model is utilized. By comparing the predicted correlation matrix with the actually observed correlation matrix, the posterior predictive discrepancy is calculated. Then, the posterior predictive discrepancies of different subjects are accumulated to obtain the cumulative energy discrepancy curve, and the local maximum points in the curve are regarded as the network structure change points. A detailed introduction to this part can be found in Wang's work [Wang *et al.*, 2024]. Change point detection parameters, empirically validated as optimal in prior studies, were applied here to ensure methodological consistency and reliability. After that, the whole time series is segmented by using the detected change points, and the best brain effective connectivity network based on the assumption of stationary time series is learned by using the improved FBS method on each time segment.

2.3 Brain Active Information

The information on the activity of brain regions is an important tool for analyzing abnormal conditions of the brain and understanding brain functions. Since the construction of brain networks using fMRI data relies on the blood oxygen level dependent (BOLD) signals attached during the data collection process. And the collection process will inevitably be affected by the head movements of subjects and equipment noise, this leads to the fact that the time series of various brain regions finally extracted contain a lot of noise. Therefore, we process the extracted time sequences before constructing the network. In order to extract brain active information, the preprocessed data are processed again. This process is shown in Fig. 2. This process mainly uses resting-state fMRI data from each subject to obtain their BOLD signal in the steady state as a baseline of brain activity. After removing the baseline signal from the preprocessed time series of each brain region, the unique active signal of each brain region in the task-state is obtained. This can effectively focus only on the active information in the task-state to avoid the influence of irrelevant factors on the network construction [Akkurt *et al.*, 2023].

Figure 2: The Process of Active Information Extraction.

To facilitate subsequent calculations, the resulting unique signals for each brain region are normalized. The activity threshold p is then set to determine the activity of each brain region at each time point. To empirically validate the threshold p, we systematically tested values in $[0.2, 0.8]$ (step size 0.05), finding $p \in [0.4, 0.55]$ yielded minimal variance and superior performance, with $p = 0.45$ selected as the optimal value for experiments. Activity is divided into three levels as shown as (1). The first is completely inactive. This state of completely inactive occurs only after human death, so it is not considered in the experiment. The second is hypoactive or inhibited state, which occurs mostly in the resting state and a few in the inhibitory effect of the brain. The third is a hyperactive state, which occurs mostly in brain regions that are activated while completing the task.

$$v_a^t = \begin{cases} Stationary & not\ considered \\ 0 & hypoactive/inhibited \\ 1 & hyperactive \end{cases} \tag{1}$$

When the activity value of brain region a is greater than or equal to the active threshold p at time t, which is $x_t^a \geq p$, the brain region a is judged to be in a hyperactive state at time t. Conversely, when the activity value of brain region a is less than the active threshold p at time t, which is $x_t^a < p$, the brain region a is judged to be in hypoactive or inhibited state at time t.

Brain Active Probability

For each pair of brain region a and brain region b, the joint active state of this pair of brain regions can be interpreted as four different situations, as shown in Fig. 3. In the Fig. 3, the dots represent different brain regions, and the colors represent different active states of the brain regions. Among them, red indicates that the brain region is in a hyperactive state, while blue indicates that the brain region is in a hypoactive or inhibited state. Besides, the corresponding joint activation probabilities are shown in Table. 1.

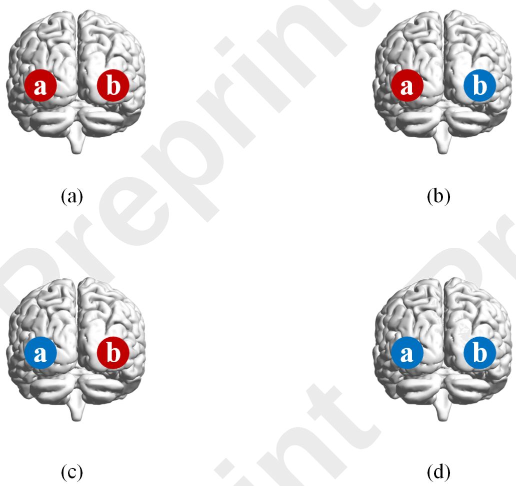


Figure 3: Four Different Situations of the Joint Active State.

		Region a	
		Active	Inactive
Region b	Active	θ_1	θ_2
	Inactive	θ_3	θ_4

Table 1: Four Cases of Pairs of Brain Regions

In Table. 1, the four elements of θ_1, θ_2, θ_3, and θ_4 are the joint activation probabilities corresponding to the above four cases in the Fig. 3, and $\theta_1 + \theta_3$, $\theta_1 + \theta_2$ are the marginal activation probabilities for brain regions a and b, respectively. In detail, the calculation formulas of the joint activation probabilities $\theta_i \; (i = 1,\ 2,\ 3,\ 4)$ are shown in (2)-(5).

$$\theta_1 = \frac{V_a^T \times V_b}{L_v} \tag{2}$$

$$\theta_2 = \frac{V_a^T \times (I - V_b)}{L_v} \tag{3}$$

$$\theta_3 = \frac{V_b^T \times (I - V_a)}{L_v} \tag{4}$$

$$\theta_4 = \frac{(I - V_a)^T \times (I - V_b)}{L_v} \tag{5}$$

Brain Hierarchy Information

The synchronism of brain region active states refers to a series of states in which pairs of brain regions are simultaneously in a hyperactive state or simultaneously in a hypoactive or inhibited state, corresponding to (a) and (b) in Fig. 3. And the corresponding asynchronism of brain region active states refers that in a pair of brain regions, one brain region is in a hyperactive state while the other brain region is in a hypoactive or inhibited state, corresponding to (c) and (d) in Fig. 3 [Suzuki *et al.*, 2018].

Some synchronization research methods have shown that stronger synchronization between two brain regions means that they are more likely to jointly complete the task of information interaction. In other words, brain regions that have synchronism in their active states are more likely to simultaneously play the roles of issuing commands or receiving commands (parent nodes or child nodes in the network) in the task[Esch *et al.*, 2020].

2.4 Network Structure Learning

The accurate construction of brain networks can provide more favorable assistance for the auxiliary diagnosis of brain diseases and offer new opportunities for researchers to conduct in-depth exploration of brain functions and unveil the mysteries of the brain [Liu *et al.*, 2024b]. Therefore, how to simulate the working mode of brain networks in a more realistic manner has always been the focus of research. Here, in view of the problems that existing methods are unable to construct time-varying brain networks and also unable to build the interaction relationships among brain regions within multiple time delays, a new higher-order non-stationary brain effective connectivity network construction method is proposed, called TSTAI. In this process, two kinds of information on the activity of brain regions are respectively integrated into the construction process to achieve a more efficient and accurate construction of brain effective connectivity networks.

Initial Condition Set Filter

Filtering the initial set of conditions before starting network structure learning is a common method to optimize methods [Yokoyama and Kitajo, 2022; Warnick *et al.*, 2018]. Here use the hierarchical information of the brain active state combined with Pearson's correlation to filter the condition set of each node.

The active states of the brain can be divided into two types, including synchronous and asynchronous activity. When paired brain regions are in a synchronous co-active or co-inhibitory state, it can be considedred that these paired brain regions are in the same hierarchical structure. According to previous studies, the regulatory effects of the parent nodes of the same target node on the target node are at the same frequency at different times [Lv *et al.*, 2023]. Therefore, nodes in the same hierarchical structure are more likely to regulate the same target node. Meanwhile, according to the traditional constructing and analyzing brain functional networks methods, the magnitude of the Pearson correlation between paired brain regions can reflect the degree of correlation between brain regions [Liu *et al.*, 2023]. That is to say, when the Pearson coefficient between brain regions is larger, these two brain regions are in a closer relationship and are more likely to have interaction effects.

In order to achieve the accurate construction of higher-order brain effective connectivity networks more efficiently, we propose a method that combines the hierarchical structure of brain active states with Pearson correlation to filter the initial parent node sets for each target node. This process first calculates the correlation matrix by using Pearson correlation, and then ranks the magnitudes of the correlations between each target node and other nodes. Then, the top 50%

of nodes associated with the target nodes are selected as the candidate condition set. After that, the candidate condition set is supplemented according to the hierarchical structure derived from the brain active states to obtain the complete set of potential parent nodes. Doing so can effectively reduce the search space in the network structure learning stage and improve efficiency. Meanwhile, it can also avoid the problem that the traditional single-condition-set screening method filters out too many correct parent nodes in the initial stage.

Improved Scoring Function

How to accurately judge the direction of brain interval connection has always been a difficult point in the construction of brain effective connectivity network [Nadji-Tehrani and Eslami, 2020].

Traditional Bayesian scoring functions, such as K2, BIC and so on, will obtain the same scores when dealing with Markov equivalence classes. At this time, the algorithm will make a random selection between $a \to b$ and $b \to a$, and at this time, the error occurrence rate is 50%. Obviously, this random selection mechanism is not advisable. Meanwhile, how to accurately handle the structures of Markov equivalence classes is an urgent problem to be solved in the process of Bayesian network structure learning. Here we use the active probability to improve the BN scoring function. This helps to achieve more precise edge orientation determination. The optimized scoring function is shown as (6).

$$J\left(G_i;\eta_i\right) = W\left(2\log P\left(D_i|G_i;\eta_i\right) - \text{constant}\right) \quad (6)$$

In (6), η_i represents an unknown set of parameters in a multi-input single-output network (subnetwork structure) for node i, W represents the scaling coefficient, which is calculated by the marginal activation probabilities as shown in (7).

$$W = \frac{\theta_1 + \theta_3}{\theta_1 + \theta_2} \quad (7)$$

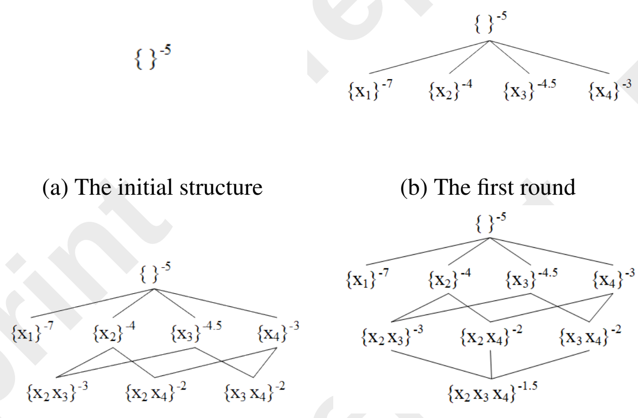
When $W > 1$, it means that brain region a activity occupies a higher priority than brain region b.At time t, the brain region that is more active in a pair of brain regions has a greater probability of playing the role of issuing commands (the parent node in network). This enlarges the score and supports the selection of networks containing edge $e_{a,b}$.

Improved Searching Process

After that, the pruning strategy is utilized in every candidate network search stage. This process removes the candidate network structure $\widehat{G}$ when the new network score $\widehat{J}$ is smaller than the original score J after calculating the score of each candidate network in each round of search process. At the same time, this candidate node is removed from the candidate conditional set. This process is shown in Fig. 4

2.5 Time Complexity Analysis

In this section, we disscuss the computational cost of our algorithm. First, we denote N as the number of brain regions and T as the length of time series. The computational cost of change point detection part of TSTAI is $O(T)$. Then in the process of higher-order network structure learning, the computational time complexity of the MISO is $O(N)$. Subsequently, during the structural learning phase for each MISO, two stages are involved: the forward/backward search, both of which exhibit a time complexity of $O(N^2)$. Meanwhile, the EM algorithm incurs a time complexity of $O(T^3)$. As mentioned above, the total computational cost of our algorithm implementation is $O(T + N(N^2 + T^3))$.



(a) The initial structure (b) The first round

(c) The second round (d) The final round

Figure 4: The Process of Pruning.

3 Materials and Results

3.1 Datasets and Preprocessing

Real Task-state Data

The data used in the experiment come from the Human Connectome Project (HCP), which is publicly available (https://db.humanconnectome.org/). Detailed introduction of data can be viewed in HCP official website (https://humanconnectome.org). The task-state fMRI (ts-fMRI) data of 89 unrelated healthy adult subjects under a block designed working memory task are obtained. The data of each subject include 405 time points, 4 block design 2-back experiments, 4 block design 0-back experiments and 4 fixed blocks.

To obtain cleaner data, a standard process for preprocessing task-state fMRI data is applied [Glasser *et al.*, 2013]. After that, the general linear model (GLM) is used to identify the significant active regions among different subjects. The regions whose Z statistics are greater than the preset threshold are selected as the regions of interest. In order to extract the time series of the region of interest, a spherical brain template is defined with the selected maximum point of local Z statistics as the spherical center and 6mm as the radius. And the average time series of all voxel time series in the region of interest is calculated. A total of 35 brain regions of interest are obtained through the above process.The information of 35 brain regions is shown in Table 2 and is sorted by brain region names in the alphabetic order.

Node	Z	MNI x	MNI y	MNI z	Brain Region Name
1	4.97	48	-58	22	Angular Gyrus.
2	9.61	36	8	12	Central Operational Cortex
3	8.27	-36	4	12	Central Operational Cortex
4	6.48	40	34	-14	Frontal Orbital Cortex
5	7.83	-12	46	46	Frontal Pole.
6	6	52	38	10	Inferior Frontal Gyrus
7	4.84	54	32	-4	Inferior Frontal Gyrus
8	4.38	-52	40	6	Inferior Frontal Gyrus
9	7.26	-48	-68	34	Inferior Parial Lobule
10	6.05	52	-70	36	Inferior Parial Lobule
11	6.18	44	-24	-20	Inferior Temporal Gyrus
12	9.54	36	-86	16	Lateral Occidental Cortex
13	8.04	-30	-80	-34	Left Crus I
14	7.6	-8	-58	-52	Left IX.
15	6.9	-22	-48	-52	Left VIIIb.
16	14.5	6	-90	-10	Lingual Gyrus.
17	10.3	30	10	58	Middle Frontal Gyrus
18	6.61	66	-30	-12	Middle Temporal Gyrus
19	4.53	-68	-34	-4	Middle Temporal Gyrus
20	14.5	18	-88	-8	Occidental Fusiform Gyrus
21	5.06	-12	-92	-2	Occidental Pole.
22	9.87	6	40	-6	Paracingulate Gyrus.
23	12	42	-16	-2	Planum Polare.
24	11.3	-40	-22	0	Planum Polare.
25	9.03	38	-26	66	Postcentral Gyrus.
26	8.31	-10	-60	14	Precuneus Cortex.
27	10.9	32	-58	-34	Right Crus I
28	8.34	32	-80	-34	Right Crus I
29	5.7	46	-60	-42	Right Crus I
30	6.41	10	-8	-14	Right Hippocampus.
31	7.69	24	-46	16	Right Lateral Ventricle
32	6.19	32	-52	2	Right Lateral Ventricle
33	6.13	0	10	-14	Subcallosal Cortex.
34	10.7	48	-44	46	Supramarginal Gyrus.
35	4.23	-50	-46	10	Supramarginal Gyrus.

Table 2: The Information of Selected Significantly Active Brain Regions

Synthetic Data

In order to evaluate the accuracy of the proposed method and the influence of different data length on network construction, the performance of the TSTAI is tested using the data of known ground truth network structure. In network structure learning section, the simulated fMRI data including 35 brain regions of different lengths as $T = \{500, 800, 1000\}$ are generated separately through a known structure network for experiments.

3.2 Experiments

In order to verify the effectiveness of the proposed method, we compare the proposed TSTAI method with advanced methods for multiple experiments use real data and simulated data. HO-BIC [Ji *et al.*, 2021] and HO-CPD-NSL [Wang *et al.*, 2024] methods are selected to carry out the experiment. The common network evaluation measures such as true positive rate (TPR), false positive rate (FPR) and dis value are selected to compare the estimated network structure with the real network structure. The calculation formulas of each evaluation measure are shown in Table 3. At the same time, the average time to repeat the construction 50 times under different length time series is also recorded as one of the measures of network construction efficiency. The results of experiments using simulated data are shown in Table 4.

Evaluation metrics	Formula
TPR	$TPR = \frac{TP}{TP+FN}$
FPR	$FPR = \frac{FP}{FP+TN}$
dis	$dis = \sqrt{FPR^2 + (1 - TPR)^2}$

Table 3: Evaluation Metrics

T	Method	TPR	FPR	dis	Time(s)
1000	HO-BIC	0.77	0.23	0.33	34085.6
	HO-CPD-NSL	0.92	0.18	0.20	**20743.3**
	TSTAI	**0.97**	**0.02**	**0.04**	22017.2
800	HO-BIC	0.83	0.11	0.20	32085.6
	HO-CPD-NSL	0.90	0.13	0.16	**17641.8**
	TSTAI	**0.94**	**0.03**	**0.07**	18382.1
500	HO-BIC	0.71	0.11	0.31	27411.4
	HO-CPD-NSL	0.91	0.14	0.17	**15819.6**
	TSTAI	**0.93**	**0.03**	**0.08**	16662.2

Table 4: The Results of Evaluation Metrics Using Different Network Structure Learning Methods

From the experimental results in Table 4, it can be seen that in the experiments of different T, the TSTAI achieves the best results in the vast majority of evaluation metrics compared with other methods. As traditional higher-order Bayesian network structure learning methods do not consider the non-stationary time-series assumption, the correctness of network construction is compared with these traditional methods only on stationary time-series. Compared with traditional higher-order Bayesian network structure learning methods, the TSTAI method has improved the accuracy of network structure learning in experiments with time-series of different lengths. Its average true positive rate has increased by 17.4%. At the same time, there has been a significant improvement in efficiency, with the average time required to construct the network being reduced by 12173.7 seconds.

Then, the TSTAI method is compared with the advanced method for constructing higher-order brain effective connectivity networks based on the non-stationary time-series assumption. It can be seen from Table 4, TSTAI can achieve more accurate network structure learning results. Under the condition of time series of different lengths, the true positive rate is increased by an average of 3.67%. It not only restores the most real edges, but also maintains the least false positive edges. However, the runtime is slightly worse than the HO-

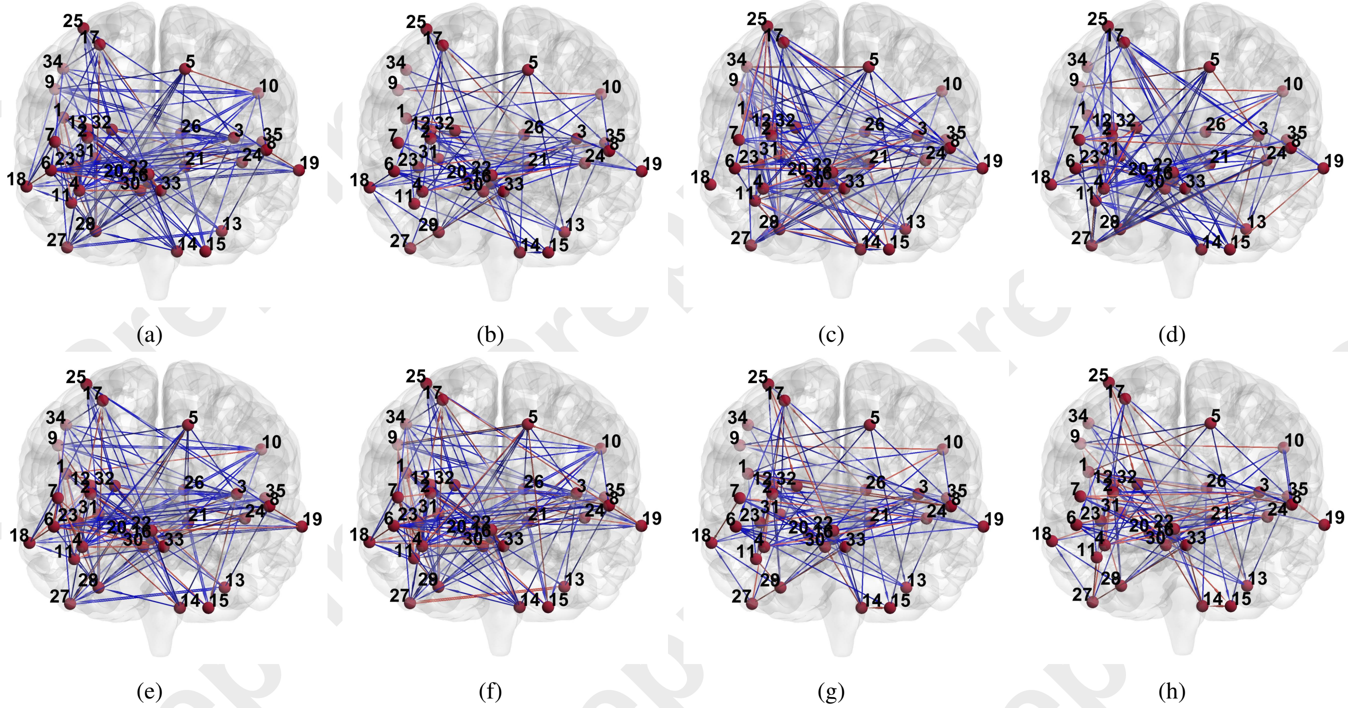


Figure 5: The Results of TSTAI for Working Memory tfMRI Data: (a), (c), (e), (f) represent brain states corresponding to 2-back working memory tasks. (b), (d), (g), (h) represent brain states corresponding to 0-back working memory tasks.

CPD-NSL method. HO-CPD-NSL get less runtime because that more false positive edges are retained during the network search. This leads network structure learning to stop with fewer rounds of search processes while accuracy is lower. Meanwhile, it can be seen from Table 4 that TSTAI maintains a high level of network construction accuracy under different time-series lengths. This also indicates that, compared with other methods, the TSTAI method exhibits better robustness when the amount of data is insufficient.

After that, the experiment using real data from HCP is conducted. The construction results of the higher-order brain effective connectivity network for a randomly selected subject are shown in Fig. 5. The (a), (c), (e), (f) represent brain states corresponding to the subject when performing 2-back working memory tasks. (b), (d), (g), (h) represent brain states corresponding to the subject when performing 0-back working memory tasks. The blue lines in Fig. 5 represent the first-order edges, and the red lines represent the higher-order edges. Here, we only considered a time delay of one unit. By comparing brain networks under different tasks, it can be seen that brain have more complex patterns of connectivity when performing more complex tasks. As can be seen from Fig. 5, the number of edges in the higher-order brain effective connectivity network of the subject when performing the 2-back task is significantly larger than that when performing the 0-back task. Consistent across all 100 subjects, 87 subjects showed increased edges in all four 2-back tasks, 11 subjects showed increased edges in three 2-back tasks, and 2 subjects showed increased edges in two 2-back tasks, which aligns with the intrinsic working mechanisms of the brain reported in current studies.

Finally, by analyzing different brain effective connectivity networks, the edges pointing from visual areas to motor areas can be observed among different subjects. At the same time, it can be observed that there exist higher-order delay relation on these edges. This is consistent with the task setting where different tasks are started by visual cues. Besides, this aligns with studies showing task-induced modulation of visual-motor pathways [Wang *et al.*, 2024].

4 Conclusion

The connectivity patterns of the brains become more intricate under task conditions, with its state continually evolving as it undertakes diverse tasks. Therefore, the single non-stationary or higher-order assumption is no longer applicable in constructing complex brain effective connectivity networks. In this paper, a novel brain effective connectivity network construction method is proposed by considering both two assumptions and combining two kinds of active information, called TSTAI. The stability and accuracy of the TSTAI are verified by simulation data under different lengths. Compared with state-of-the-art methods, the TSTAI achieves the best results in most metrics. Afterwards, the ability of the TSTAI to be applied in practical problems is further verified using real data. While initially applied to brain network modeling, the TSTAI framework is inherently generalizable to other domains (e.g., finance, molecular biology) by redefining domain-specific parameters, offering a versatile tool for time-series regulatory network inference.

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