Analysing sex difference on the correlates between ADHD and sleep, comorbidity, and significant brain traits by multi-sample structural equation model

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Abstract
Current studies has found many evidences of correlation between ADHD and other major psychiatric disorders, ADHD and sleep problems, or ADHD and the traits from multiple modal brain images. Moreover, there is significantly different prevalence of ADHD between the groups of sex, which suggesting the different pathogenesis. In this study, we aim to explore the relationships between ADHD and three key factors, including mental disease, and sleep, and brain resting-state MRI (rsfMRI) findings within each group of single sex, and, furthermore, verify how these factors may differentially influence ADHD patients of different genders. By applying multiple sample structural equation models (SEMs) on simulation data and real data collected from the Adolescent Brain Cognition Development (ABCD) study.

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1 Introduction

Attention Deficit/Hyperactivity Disorder (ADHD), characterizing persistent pattern of inattention, hyperactivity, and impulsive behavior, is a common mental disorder impacting from children to adults worldwide[7].

1.1 ADHD and mental health

In recent years, the relationship between ADHD and major mental diseases has been recognized. Studies have shown that individuals with ADHD have an elevated risk of developing various mental disorders[10], such as oppositional defiant disorder, obsessive-compulsive disorder, bipolar disorder, etc. In clinical practice, it is crucial to consider the co-occurrence of ADHD and psychosis, as the presence of both may lead to more severe symptoms and poorer outcomes. Moreover, distinguishing between ADHD and early psychosis is essential for appropriate diagnosis and treatment[10].

1.2 ADHD and Sleep

Sleep disturbances are frequently reported in individuals with ADHD, leading to a growing interest in understanding the relationship between ADHD and sleep quality[2]. Studies have suggested that ADHD patients experience higher rates of insomnia, sleep-disordered breathing, restless leg syndrome, and other sleep-related problems, compared to individuals without ADHD[6].

1.3 ADHD and Brain MRI

Neuro-imaging studies have provided valuable insights into the neural correlates of ADHD. Brain MRI studies have identified structural and functional differences in ADHD patients compared to control subjects[8]. These findings have advanced our understanding of the neurobiological basis of ADHD and may contribute to the development of more targeted and effective treatments.

1.4 ADHD related to gender

Given the complexity and heterogeneity of ADHD, it is important to consider factors that may moderate the relationships between ADHD and the three aforementioned factors. One such important factor is gender, which has been confirmed to greatly influence the progress of various mental disorders[5]. ADHD also shows significant different morbidity risk between gender: ADHD is more commonly diagnosed in males[3]. However, females with ADHD often present with distinct symptom profiles and may be under-diagnosed or misdiagnosed[7].

1.5 Study design

We propose a study to explore how the relationships between ADHD, major mental diseases, sleep problems, and rsfMRI functional connectivity (FC) findings may differ between male and female patients by multiple sample structural equation models. This investigation could provide valuable insights into the potential influence of gender on the clinical presentation and

neurobiology of ADHD. It could also contribute to the development of more personalized and effective treatment strategies for individuals with ADHD.

2 Data set

ABCD study is the most extensive long-term study of brain development and child health in the United States, which recruited 11,878 children ages 9–10 in 21 research sites across the United States and collect various MR imaging data, genomics data, and the scales and questionnaires of mental health, physical health, demographics, and neurocognition[1]. Due to our previous research, we possess the accessibility of the ABCD study dataset, 2.0.1, released in 2019.

Here, we take advantages of three tabulated data, including the Child Behavior Checklist (CBCL) for evaluating ADHD and other related psychiatric disorders' severities, the Sleep Disturbance Scale (SDS) for evaluating the sleep problems, and the ADHD associated functional connectivities that has been found by our previous multimodal neuroimaging study.

All these data are available by submitting an application to ABCD Consortium, and the full and detailed dataset descriptions can be found on the website of NDA.

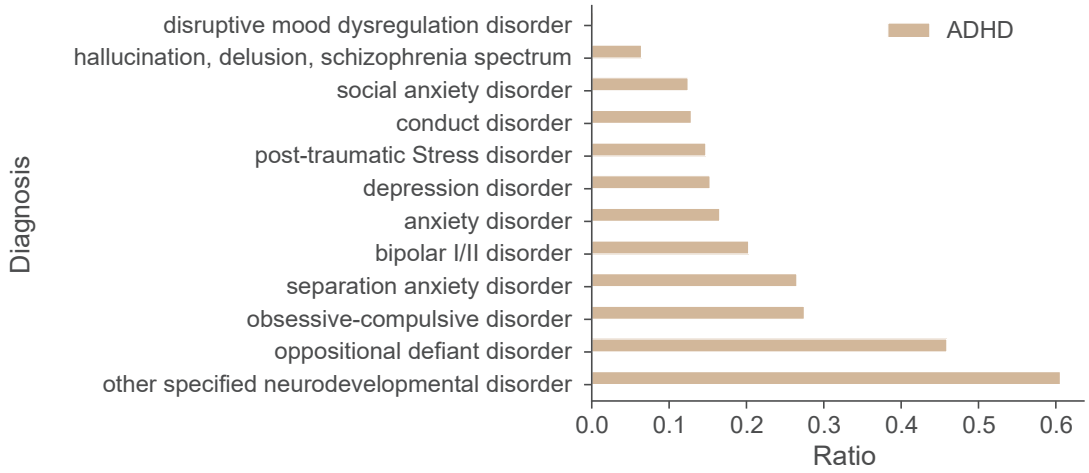

Figure 1: Comorbidity ratio in ADHD cases (analysed from the scales of KSADS in ABCD study, modified from a previous study[11])

2.1 ADHD and other major psychiatric problems

The Child Behavior Checklist (CBCL) is a widely-used parent-report questionnaire designed to assess behavioral and emotional disorders in children and adolescents, and has proven to be a valuable tool for informing treatment planning, and monitoring progress over time.

The psychiatry items associated to ADHD, as comorbidities of ADHD are shown in Figure 1, used in this study are listed in Table 1, all of which are converted to ordered categorical variables in $\{1, 2, 3\}$, representing "non-clinical symptom", "at risk", "significant clinical syndrome", respectively, according to the conventions[1;4].

Table 1: The measurements related to the outcome of interest (η: z_1) and major psychiatric disorders (ξ_1: $z_{2:6}$)

Notation	description
z_{1i}	Orderly categorized ADHD CBCL DSM5 Scale (t-score)[1,2]
z_{2i}	Orderly categorized Opposit CBCL DSM5 Scale (t-score)
z_{3i}	Orderly categorized Obsessive-Compulsive Problems (OCD) CBCL Scale2007 Scale (t-score)
z_{4i}	Orderly categorized AnxDisord CBCL DSM5 Scale (t-score)
z_{5i}	Orderly categorized Conduct CBCL DSM5 Scale (t-score)
z_{6i}	Orderly categorized Depress CBCL DSM5 Scale (t-score)

1. T-scores are continuous values modified from the raw scores that are the summation of related items in CBCL considering sex and age.
2. In this study, the original t-scores are converted to ordered categorical data by 1 = 50-54 (non-clinical symptom); 2 = 55-64 (at risk); 3 = more than 65 (significant clinical syndrome). (the same below).

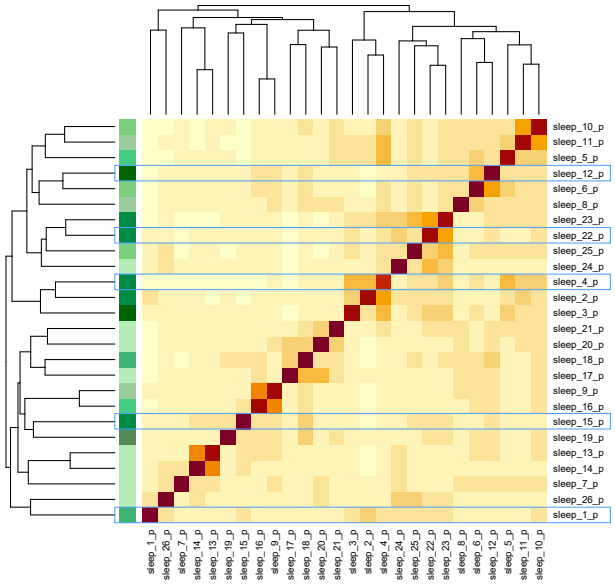

Figure 2: The heatmap of correlation between 26 sleep related items

The columns and rows are clustered by hierarchical clustering and the green bar on left of the heatmap is the variance of each item. We select the most variable in each cluster, say the annotated five in blue long rectangles.

Table 2: The selected variables that indicate the sleep problem (latent variable ξ_2: $z_{7:11}$)

ABCD var.name	notation	questions
`sleep_1_p`	z_{7i}	How many hours of sleep does your child get on most nights?[1]
`sleep_4_p`	z_{8i}	The child has difficulty getting to sleep at night.[2]
`sleep_12_p`	z_{9i}	The child has frequent twitching or jerking of legs while asleep or often changes position during the night or kicks the covers off the bed.[2]
`sleep_15_p`	z_{10i}	The child snores.[2]
`sleep_22_p`	z_{11i}	The child is unusually difficult to wake up in the morning.[2]

1. 1 = 9-11 hours; 2 = 8-9 hours; 3 = 7-8 hours; 4 = 5-7 hours; 5 = Less than 5 hours.
2. 1 = Never; 2 = Occasionally (once or twice per month or less); 3 = Sometimes (once or twice per week); 4 = Often (3 or 5 times per week); 5 = Always (daily).

2.2 Sleep problem

The Sleep Disturbance Scale (SDS) is a self-report questionnaire or a parent-report questionnaire designed to assess various sleep disturbances in children and adolescents. The scale aims to evaluate the frequency and severity of sleep problems, providing valuable information for clinicians and researchers to understand and treat sleep-related issues in pediatric populations.

Noticing there are 26 valid items in the SDS, for simplicity, we only focus on the 5 most informative items which can represent the status of sleep disturbance as shown in Figure 2, and the detials of these five items are listed in Table 2. Generally, the larger the value in $\{1, 2, 3, 4, 5\}$ is, the more problematic the sleep status is.

Table 3: ADHD related functional connectivities (ξ_3: $z_{12:17}$)

Notation	description
z_{12i}	Ventral attention network and auditory network Corr $(+)^{1,2,3}$
z_{13i}	Left pallidum and default network Corr $(+)$
z_{14i}	Left thalamus proper and salience network Corr $(+)$
z_{15i}	Right cerebellum cortex and default network Corr $(-)$
z_{16i}	Left cerebellum cortex and dorsal attention network Corr $(+)$
z_{17i}	Left cerebellum cortex and sensorimotor mouth network $(-)$

1. The average correlation values were calculated between paired cortical function network ROIs and then transformed to z-score.
2. 1 = Never; 2 = Occasionally (once or twice per month or less); 3 = Sometimes (once or twice per week); 4 = Often (3 or 5 times per week); 5 = Always (daily).
3. "+": increased and "−": decreased connectivity found by the mentioned previous study.

2.3 Brain traits of function connectivity

For image based brain traits, we focus on functional connectivity between cortical function networks or/and subcortical regions by rsfMRI. The average correlation values were calculated between paired cortical function network ROIs, representing the strength of FC[9]. FC reflects a straightforward, observational measure of functional relationships between the target networks, which has been a universal tool to analyze ADHD.

From our previous study[11], we choose six most frequently selected FCs, listed in Table 3, which are continuous values normatively falling between $[-1, 1]$. Following the official recommendation, the subjects that did not pass the quality control of structural MRI and with less than 375 frames in rsfMRI are excluded from further analysis.

The subjects with any missing field are also excluded, and finally 3,464 male and 3,109 female subjects are enrolled in the group difference analysis.

3 Model Specification

With the notations of observed and latent variables defined in the previous section, this section specifies the multiple sample SEMs with distinct constraints for model comparison. In the following multiple sample SEM analysis, we define two groups, $g = 1$ as male and $g = 2$ as female.

3.1 Multiple sample SEM

The measurement equation (ME) and structural equation (SE) in multiple sample SEM are specified as follow

$$\boldsymbol{v}_i^{(g)} = \boldsymbol{\mu}^{(g)} + \boldsymbol{\Lambda}^{(g)}\boldsymbol{\omega}_i^{(g)} + \boldsymbol{\varepsilon}_i^{(g)} \tag{1}$$

$$\eta_i^{(g)} = \boldsymbol{\Gamma}^{(g)}\boldsymbol{\xi}_i^{(g)} + \delta_i^{(g)} \tag{2}$$

for $g = 1, 2$ and $i = 1, \cdots, N_g$, where N_1=3,464, N_2=3,109, $\boldsymbol{v}_i^{(g)}, \boldsymbol{\mu}_i^{(g)}, \boldsymbol{\varepsilon}_i^{(g)} \in \mathbb{R}^{17}$, and the matrices and vectors have the following structures:

$$\boldsymbol{\Lambda}^{(g)} = \begin{bmatrix} 1 & \mathbf{0} & \mathbf{0} & \mathbf{0} \\ 0 & \boldsymbol{\lambda}_2^{(g)\mathsf{T}} & \mathbf{0} & \mathbf{0} \\ 0 & \mathbf{0} & \boldsymbol{\lambda}_3^{(g)\mathsf{T}} & \mathbf{0} \\ 0 & \mathbf{0} & \mathbf{0} & \boldsymbol{\lambda}_4^{(g)\mathsf{T}} \end{bmatrix}^{\mathsf{T}}, \ \boldsymbol{\lambda}_2^{(g)} = \begin{bmatrix} 1 & \lambda_{3,2}^{(g)} & \lambda_{4,2}^{(g)} & \lambda_{5,2}^{(g)} & \lambda_{6,2}^{(g)} \end{bmatrix}^{\mathsf{T}}$$

$$\boldsymbol{\lambda}_3^{(g)} = \begin{bmatrix} 1 & \lambda_{8,3}^{(g)} & \lambda_{9,3}^{(g)} & \lambda_{10,3}^{(g)} & \lambda_{11,3}^{(g)} \end{bmatrix}^{\mathsf{T}}, \ \boldsymbol{\lambda}_4^{(g)} = \begin{bmatrix} 1 & \lambda_{13,4}^{(g)} & \lambda_{14,4}^{(g)} & \lambda_{15,4}^{(g)} & \lambda_{16,4}^{(g)} & \lambda_{17,4}^{(g)} \end{bmatrix}^{\mathsf{T}}$$

$$\boldsymbol{\omega}_i^{(g)} = \begin{bmatrix} \eta_i^{(g)} & \boldsymbol{\xi}_i^{(g)\mathsf{T}} \end{bmatrix}^{\mathsf{T}}, \ \boldsymbol{\xi}_i^{(g)} = \begin{bmatrix} \xi_{1i}^{(g)} & \xi_{2i}^{(g)} & \xi_{3i}^{(g)} \end{bmatrix}^{\mathsf{T}}, \text{ and } \boldsymbol{\Gamma}^{(g)} = \begin{bmatrix} \gamma_1^{(g)} & \gamma_2^{(g)} & \gamma_3^{(g)} \end{bmatrix}$$

For the ordered categorical measurements, suppose that $\boldsymbol{v}_i^{(g)} = \begin{bmatrix} \boldsymbol{y}_i^{(g)\mathsf{T}} & \boldsymbol{x}_i^{(g)\mathsf{T}} \end{bmatrix}^{\mathsf{T}}$, where $\boldsymbol{z}_{12:17,i}^{(g)} = \boldsymbol{x}_i^{(g)}$ is a subvector of observable continuous responses, and $\boldsymbol{y}_i^{(g)} \in \mathbb{R}^{11}$ is an subvector of unobservable continuous responses whose information is reflected by its corresponding

ordered categorical variable $\boldsymbol{z}_{1:11,i}^{(g)}$ by a common threshold referring to group 1 (male).

$$z_{mi}^{(g)} = a \text{ if } \alpha_{m,a}^{(1)} \le y_{mi}^{(g)} < \alpha_{m,a+1}^{(1)},\ a = 0, \cdots, b_m,$$
$$b_m = \begin{cases} 3 & \text{for } m = 1,2,3,4,5,6 \\ 5 & \text{for } m = 7,8,9,10,11 \end{cases},$$

where the thresholds are fixed by $\alpha_{m,0}^{(1)} = -\infty, \alpha_{m,b_m+1}^{(1)} = \infty$, and $\alpha_{m,a}^{(1)} = \Phi^{-1}(f_{m,a}^{(1)})$ for other a of categorical labels, and $f_{m,a}^{(1)}$ is the empirical accumulative frequency for class a in group 1.

Moreover, besides the basic assumption of SEM, in the non-constrained case, the variables in SEM are assumed to follow the distributions below

- **basic assumptions**:

$$\begin{aligned} &\boldsymbol{\varepsilon}_i^{(g)} \overset{\text{iid}}{\sim} \mathcal{N}[\mathbf{0}, \boldsymbol{\Psi}_{\varepsilon}^{(g)}], \quad \boldsymbol{\Psi}_{\varepsilon}^{(g)} = \text{diag}[\psi_{\epsilon 1}^{(g)}, \cdots, \psi_{\varepsilon 17}^{(g)}] \\ &\boldsymbol{\xi}_i^{(g)} \overset{\text{iid}}{\sim} \mathcal{N}[\mathbf{0}, \boldsymbol{\Phi}^{(g)}], \quad \boldsymbol{\Phi}^{(g)} \in \mathbb{R}^{3\times 3} \\ &\delta_i^{(g)} \overset{\text{iid}}{\sim} \mathcal{N}[\mathbf{0}, \psi_{\delta}^{(g)}], \quad \delta_i^{(g)} \perp\!\!\!\perp \boldsymbol{\xi}_i^{(g)},\ \boldsymbol{\varepsilon}_i^{(g)} \perp\!\!\!\perp \boldsymbol{\omega}_i^{(g)},\ \boldsymbol{\varepsilon}_i^{(g)} \perp\!\!\!\perp \boldsymbol{\delta}_i^{(g)} \end{aligned}$$

- **special assumptions**

$$\begin{aligned} {\psi_{\varepsilon k}^{(g)}}^{-1} &\sim \text{Gamma}[\alpha_{0\varepsilon k}^{(g)}, \beta_{0\varepsilon k}^{(g)}], \quad \boldsymbol{\Lambda}_k^{(g)} \sim \mathcal{N}[\boldsymbol{\Lambda}_{0k}^{(g)}, \mathbf{H}_{0yk}^{(g)}],\ k = 1, \cdots, 17 \\ {\psi_{\delta}^{(g)}}^{-1} &\sim \text{Gamma}[\alpha_{0\delta}^{(g)}, \beta_{0\delta}^{(g)}], \quad \boldsymbol{\Gamma}^{(g)} \sim \mathcal{N}[\boldsymbol{\Gamma}_0^{(g)}, \mathbf{H}_{0\omega}^{(g)}], \\ \boldsymbol{\mu}^{(g)} &\sim \mathcal{N}[\boldsymbol{\mu}_0^{(g)}, \boldsymbol{\Sigma}_0^{(g)}], \quad {\boldsymbol{\Phi}^{(g)}}^{-1} \sim \mathcal{W}_3[\mathbf{R}_0^{(g)}, \rho_0^{(g)}],\ g = 1, 2 \end{aligned}$$

3.2 Prior

Since such study has not been conducted yet, no much prior information can be retrieved, so we set a general priors causing relatively large variance as shown below.

$$\boldsymbol{\mu}_0^{(g)} = \mathbf{0},\ \boldsymbol{\Sigma}_0^{(g)} = 2\mathbf{I},\ \boldsymbol{\Lambda}_{0k}^{(g)} = \mathbf{0},\ \mathbf{H}_{0yk}^{(g)} = 2\mathbf{I},\ \boldsymbol{\Gamma}_0^{(g)} = \mathbf{0},\ \mathbf{H}_{0\omega}^{(g)} = 2\mathbf{I},$$
$$\alpha_{0\varepsilon k}^{(g)} = 6,\ \beta_{0\varepsilon k}^{(g)} = 4,\ \alpha_{0\delta}^{(g)} = 6,\ \beta_{0\delta}^{(g)} = 4,\ \mathbf{R}_0^{(g)} = \begin{bmatrix} 5 & 2 & 2 \\ 2 & 5 & 2 \\ 2 & 2 & 5 \end{bmatrix},\ \rho_0^{(g)} = 10,$$
$$g = 1, 2,\quad k = 1, \cdots, 17.$$

3.3 Hypotheses

To investigate the mechanism underlying the ADHD difference between genders, we come up with the hypothesis the loadings in ME are invariant ($\mathcal{M}_2$) between groups and the relationship among latent factors and factor loadings are both invariant ($\mathcal{M}_3$), and compare them with the unconstrained model ($\mathcal{M}_1$) by DIC provided by `WinBUGS`.

$$\mathcal{M}_1 : \text{no constraints}$$
$$\mathcal{M}_2 : \boldsymbol{\Lambda}^{(1)} = \boldsymbol{\Lambda}^{(2)} = \boldsymbol{\Lambda},$$
$$(\boldsymbol{\Lambda}_k \sim \mathcal{N}[\boldsymbol{\Lambda}_{0k}, \mathbf{H}_{0yk}],\ k = 1, \cdots, 17)$$
$$\mathcal{M}_3 : \boldsymbol{\Lambda}^{(1)} = \boldsymbol{\Lambda}^{(2)} = \boldsymbol{\Lambda},\ \boldsymbol{\Phi}^{(1)} = \boldsymbol{\Phi}^{(2)} = \boldsymbol{\Phi},$$
$$(\boldsymbol{\Lambda} \text{ the same with above},\ \boldsymbol{\Phi}^{-1} \sim \mathcal{W}_3[\mathbf{R}_0, \rho_0])$$

4 Results

4.1 Verification on simulation study

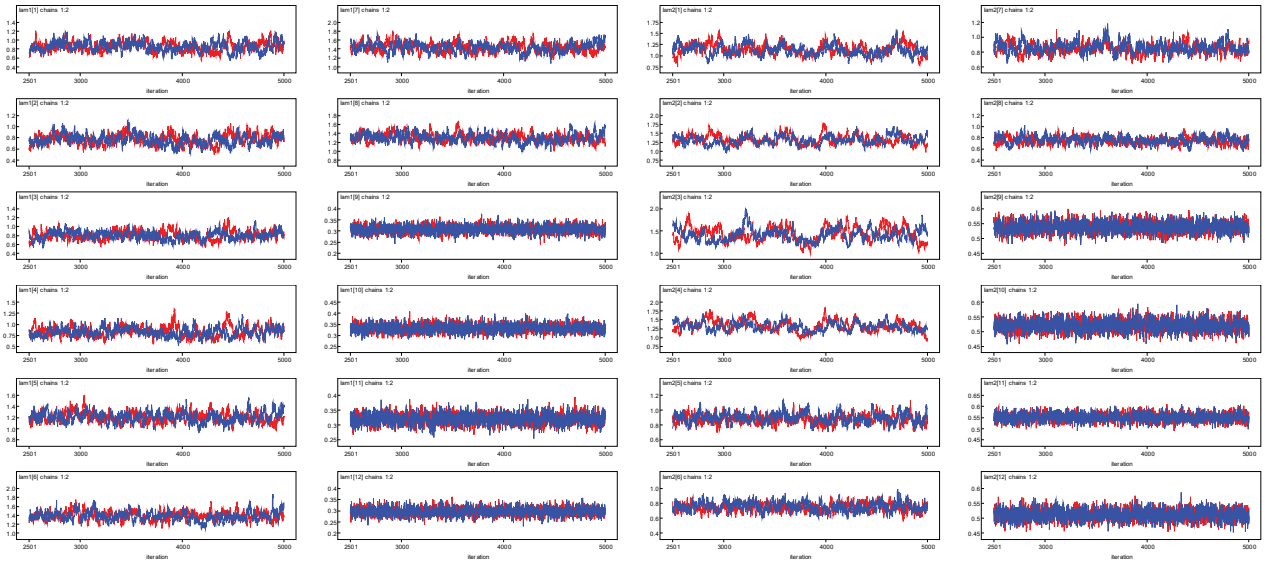

Figure 3: Simulation chains of λ's from different initial values which converge well

To verify our model and codes, 5 repetitive simulation studies are conducted. In each repetition, 1,000 samples was generated for each group and so did 5,000 iterations for estimating the unknown parameters. The other experiment settings keep the same with our real data:

- two groups and the same numbers of variables are set for the multiple sample SEM simulations;
- $z_{1:6}$ are ordered categorical variables with three classes with unbalanced percentages 7:2:1;
- $z_{7:11}$ are ordered categorical variables with five classes with unbalanced percentages 6:2:1: 0.5:0.5; and
- $z_{12:17}$ are continuous variable normally distributed.

Figure 3 shows two simulation chains of the factor loading λ's from distinct initial values converges together, and we can see with the information increasing, the number of ordered categories from 3 to 5 and to infinity (continuous), the estimation performance increases and converges better and better. The true values and evaluation, including bias and RMSE, of estimated value of unknown parameters are summerized in Tables 4 (Part 1/2) and 5 (Part 2/2). Generally, both bias and RMSE for all parameters are very small, verifying the validity of the model and codes.

Table 4: Evaluation of simulation study (Part 1/2)

	$g=1$			$g=2$		
parameter	true value	bias	RMSE	true value	bias	RMSE
$\mu_1^{(g)}$	0.1	0.02	0.04	0	0.00	0.05
$\mu_2^{(g)}$	0.1	0.00	0.06	0	0.05	0.10
$\mu_3^{(g)}$	0.1	-0.02	0.06	0	-0.06	0.08
$\mu_4^{(g)}$	0.1	0.01	0.07	0	0.02	0.04
$\mu_5^{(g)}$	0.1	0.00	0.10	0	0.04	0.08
$\mu_6^{(g)}$	0.1	0.00	0.05	0	-0.01	0.05
$\mu_7^{(g)}$	0.1	0.02	0.05	0	-0.02	0.03
$\mu_8^{(g)}$	0.1	-0.03	0.06	0	-0.02	0.05
$\mu_9^{(g)}$	0.1	-0.07	0.10	0	-0.03	0.07
$\mu_{10}^{(g)}$	0.1	0.03	0.05	0	0.01	0.04
$\mu_{11}^{(g)}$	0.1	-0.01	0.06	0	-0.05	0.07
$\mu_{12}^{(g)}$	0.1	0.01	0.02	0	0.04	0.05
$\mu_{13}^{(g)}$	0.1	0.01	0.01	0	0.01	0.02
$\mu_{14}^{(g)}$	0.1	0.00	0.02	0	0.02	0.03
$\mu_{15}^{(g)}$	0.1	0.00	0.01	0	0.01	0.02
$\mu_1^{(g)}6$	0.1	-0.01	0.01	0	0.00	0.02
$\mu_{17}^{(g)}$	0.1	0.01	0.01	0	0.02	0.03
$\lambda_{3,2}^{(g)}$	0.9	-0.02	0.06	1.1	0.09	0.13
$\lambda_{4,2}^{(g)}$	0.8	-0.02	0.07	1.2	0.07	0.14
$\lambda_{5,2}^{(g)}$	0.8	0.01	0.05	1.3	0.07	0.22
$\lambda_{6,2}^{(g)}$	0.7	0.03	0.07	1.2	0.08	0.17
$\lambda_{8,3}^{(g)}$	1.1	0.09	0.12	0.9	0.00	0.06
$\lambda_{9,3}^{(g)}$	1.2	0.13	0.13	0.8	0.04	0.08
$\lambda_{10,3}^{(g)}$	1.3	0.06	0.12	0.8	0.02	0.04
$\lambda_{11,3}^{(g)}$	1.2	0.10	0.12	0.7	0.06	0.11
$\lambda_{13,4}^{(g)}$	0.3	0.01	0.02	0.5	0.01	0.02
$\lambda_{14,4}^{(g)}$	0.3	0.02	0.03	0.5	0.01	0.02
$\lambda_{15,4}^{(g)}$	0.3	0.02	0.03	0.5	0.01	0.02
$\lambda_{16,4}^{(g)}$	0.3	0.02	0.03	0.5	0.00	0.01
$\lambda_{17,4}^{(g)}$	0.3	0.01	0.01	0.5	0.00	0.01

Table 5: Evaluation of simulation study (Part 2/2)

	$g=1$			$g=2$		
parameter	true value	bias	RMSE	true value	bias	RMSE
$\psi_{\varepsilon 1}^{(g)}$	1	-0.25	0.25	0.7	-0.13	0.13
$\psi_{\varepsilon 2}^{(g)}$	1	-0.07	0.12	0.7	-0.03	0.15
$\psi_{\varepsilon 3}^{(g)}$	1	0.05	0.08	0.7	0.08	0.12
$\psi_{\varepsilon 4}^{(g)}$	1	0.01	0.12	0.7	-0.01	0.06
$\psi_{\varepsilon 5}^{(g)}$	1	0.13	0.20	0.7	0.04	0.09
$\psi_{\varepsilon 6}^{(g)}$	1	0.02	0.11	0.7	0.03	0.10
$\psi_{\varepsilon 7}^{(g)}$	1	-0.05	0.09	0.7	0.00	0.04
$\psi_{\varepsilon 8}^{(g)}$	1	0.01	0.06	0.7	-0.01	0.08
$\psi_{\varepsilon 9}^{(g)}$	1	0.08	0.11	0.7	0.02	0.06
$\psi_{\varepsilon 10}^{(g)}$	1	-0.02	0.10	0.7	-0.02	0.07
$\psi_{\varepsilon 11}^{(g)}$	1	0.08	0.11	0.7	-0.03	0.07
$\psi_{\varepsilon 12}^{(g)}$	0.2	0.04	0.04	0.2	0.01	0.02
$\psi_{\varepsilon 13}^{(g)}$	0.2	0.00	0.01	0.2	0.01	0.01
$\psi_{\varepsilon 14}^{(g)}$	0.2	0.00	0.01	0.2	0.00	0.00
$\psi_{\varepsilon 15}^{(g)}$	0.2	0.01	0.01	0.2	0.00	0.01
$\psi_{\varepsilon 16}^{(g)}$	0.2	0.00	0.01	0.2	0.01	0.01
$\psi_{\varepsilon 17}^{(g)}$	0.2	0.01	0.01	0.2	0.01	0.01
$\gamma_1^{(g)}$	0.5	0.00	0.06	0.5	0.00	0.03
$\gamma_2^{(g)}$	0.2	0.05	0.07	0.2	0.03	0.09
$\gamma_3^{(g)}$	0.6	0.08	0.08	0.6	0.02	0.10
$\Phi_{11}^{(g)}$	1	0.02	0.11	1	-0.05	0.15
$\Phi_{12}^{(g)}$	-0.2	0.00	0.03	-0.2	0.01	0.04
$\Phi_{13}^{(g)}$	0	0.00	0.04	0	0.00	0.02
$\Phi_{22}^{(g)}$	1	-0.10	0.14	1	-0.03	0.08
$\Phi_{23}^{(g)}$	-0.5	0.03	0.05	-0.5	0.02	0.03
$\Phi_{33}^{(g)}$	1	-0.05	0.07	1	-0.05	0.05
$\psi_{\delta}^{(g)}$	0.5	0.25	0.26	0.5	0.10	0.12

4.2 Model selection and parameters estimation on real data

By fitting the above real data on the three models ($\mathcal{M}_1, \mathcal{M}_2, \mathcal{M}_3$), we can get the DIC values for each, which are displayed in Table 6. We can see $\mathcal{M}_1$ has the smallest DIC by absolute advantage, so we can claim the factor loadings and relationship among the latent factors representing psychiatric problem, sleep problem, and functional connectivity are different between genders.

Based on this result, we estimate the specific factor loadings and latent covariance on the unconstrained model, $\mathcal{M}_1$, and obtain the summary table, Table 7. Figure 4 shows the convergence of model, also taking λ's for examples, and similar pattern of estimation with simulation study. Table 8 shows the correlation between these three factors, which are very similar between gender.

Table 6: The DICs of model 1-3

model	$\mathcal{M}_1$	$\mathcal{M}_2$	$\mathcal{M}_3$
DIC	95358.3	97448	96485.7

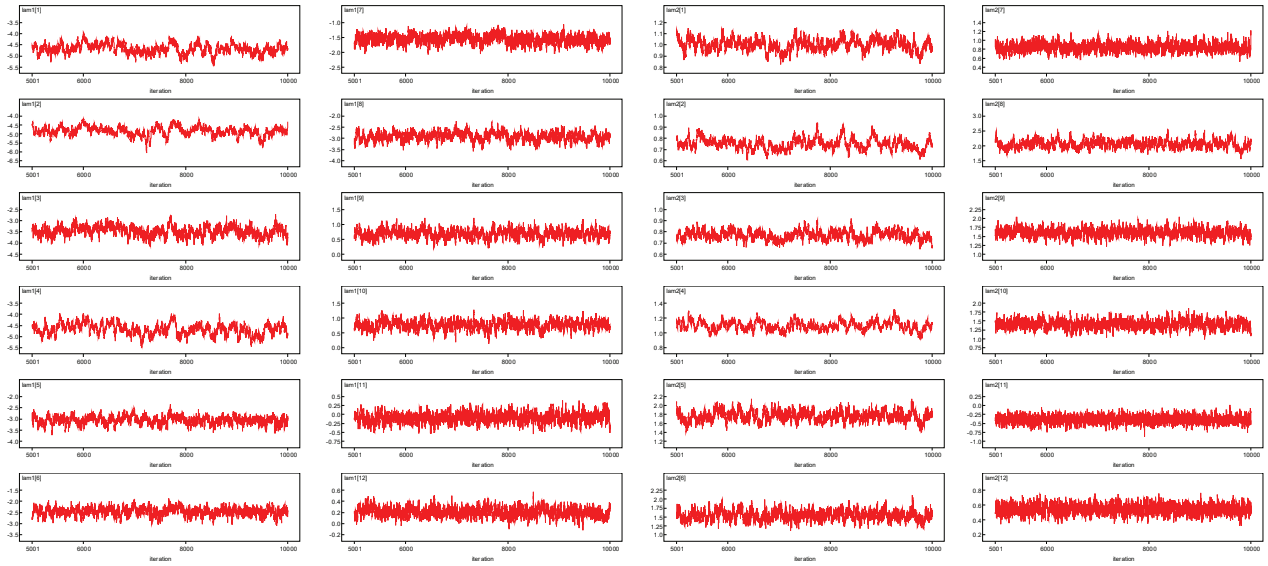

Figure 4: The chain of λ's estimation on real data

5 Discussion and conclusion

Notice that the correlation $\hat{\rho}_{ab}^{(g)}$ among latent factors are only slightly different between groups even though the estimated covariances are greatly different among groups, which may imply the female are more vulnerable to psychiatric and sleep problem than the male, but in a long run, these factors connected to each other in a human being level, which shows a similar pattern between genders.

From the estimation results, it is interesting to note that the loading matrix $\mathbf{\Lambda}^{(g)}$'s are very different and even with opposite effects between genders, which may imply the significant heterogeneity underlying the ADHD symptoms and the "real" abnormalities that leading the

Table 7: Add caption

	$g=1$		$g=2$			$g=1$		$g=2$	
parameter	mean	SD	mean	SD	parameter	mean	SD	mean	SD
$\mu_1^{(g)}$	-0.018	0.032	-0.170	0.040	$\psi_{\varepsilon 1}^{(g)}$	0.245	0.034	0.240	0.035
$\mu_2^{(g)}$	-0.163	0.035	-0.273	0.035	$\psi_{\varepsilon 2}^{(g)}$	1.646	0.095	0.384	0.031
$\mu_3^{(g)}$	0.014	0.028	-0.071	0.031	$\psi_{\varepsilon 3}^{(g)}$	0.281	0.021	0.393	0.028
$\mu_4^{(g)}$	-0.005	0.042	0.205	0.038	$\psi_{\varepsilon 4}^{(g)}$	0.274	0.025	0.202	0.017
$\mu_5^{(g)}$	0.018	0.042	0.147	0.034	$\psi_{\varepsilon 5}^{(g)}$	0.588	0.047	0.305	0.025
$\mu_6^{(g)}$	0.010	0.032	-0.164	0.037	$\psi_{\varepsilon 6}^{(g)}$	0.295	0.024	0.322	0.027
$\mu_7^{(g)}$	-0.029	0.023	-0.007	0.021	$\psi_{\varepsilon 7}^{(g)}$	1.145	0.046	0.861	0.036
$\mu_8^{(g)}$	0.004	0.020	0.087	0.019	$\psi_{\varepsilon 8}^{(g)}$	0.612	0.031	0.525	0.026
$\mu_9^{(g)}$	0.004	0.031	-0.205	0.042	$\psi_{\varepsilon 9}^{(g)}$	0.750	0.045	0.945	0.068
$\mu_{10}^{(g)}$	-0.001	0.024	0.001	0.025	$\psi_{\varepsilon 10}^{(g)}$	0.902	0.044	0.941	0.046
$\mu_{11}^{(g)}$	0.007	0.028	0.019	0.030	$\psi_{\varepsilon 11}^{(g)}$	0.643	0.040	0.665	0.041
$\mu_{12}^{(g)}$	0.071	0.002	0.065	0.002	$\psi_{\varepsilon 12}^{(g)}$	0.008	0.000	0.009	0.000
$\mu_{13}^{(g)}$	0.107	0.004	0.116	0.005	$\psi_{\varepsilon 13}^{(g)}$	0.060	0.002	0.052	0.002
$\mu_{14}^{(g)}$	0.084	0.004	0.085	0.005	$\psi_{\varepsilon 14}^{(g)}$	0.062	0.002	0.056	0.002
$\mu_{15}^{(g)}$	0.007	0.005	0.012	0.005	$\psi_{\varepsilon 15}^{(g)}$	0.076	0.002	0.067	0.002
$\mu_1^{(g)}6$	-0.025	0.003	-0.025	0.003	$\psi_{\varepsilon 16}^{(g)}$	0.030	0.001	0.025	0.001
$\mu_{17}^{(g)}$	-0.071	0.005	-0.076	0.005	$\psi_{\varepsilon 17}^{(g)}$	0.071	0.002	0.060	0.002
$\lambda_{3,2}^{(g)}$	-4.675	0.222	1.002	0.053	$\gamma_1^{(g)}$	-3.823	0.253	0.874	0.068
$\lambda_{4,2}^{(g)}$	-4.843	0.254	0.751	0.050	$\gamma_2^{(g)}$	-0.526	0.211	0.356	0.158
$\lambda_{5,2}^{(g)}$	-3.464	0.222	0.770	0.042	$\gamma_3^{(g)}$	0.345	0.458	0.396	0.473
$\lambda_{6,2}^{(g)}$	-4.670	0.252	1.096	0.061	$\Phi_{11}^{(g)}$	0.033	0.002	0.630	0.051
$\lambda_{8,3}^{(g)}$	-3.056	0.182	1.768	0.116	$\Phi_{12}^{(g)}$	0.024	0.002	0.177	0.014
$\lambda_{9,3}^{(g)}$	-2.456	0.184	1.548	0.139	$\Phi_{13}^{(g)}$	0.001	0.000	0.001	0.002
$\lambda_{10,3}^{(g)}$	-1.556	0.151	0.848	0.096	$\Phi_{22}^{(g)}$	0.042	0.004	0.099	0.010
$\lambda_{11,3}^{(g)}$	-2.912	0.195	2.060	0.139	$\Phi_{23}^{(g)}$	0.001	0.000	0.002	0.001
$\lambda_{13,4}^{(g)}$	0.689	0.152	1.610	0.120	$\Phi_{33}^{(g)}$	0.006	0.000	0.006	0.000
$\lambda_{14,4}^{(g)}$	0.767	0.155	1.409	0.120	$\psi_{\delta}^{(g)}$	0.237	0.035	0.233	0.035
$\lambda_{15,4}^{(g)}$	-0.093	0.139	-0.393	0.109					
$\lambda_{16,4}^{(g)}$	0.209	0.086	0.545	0.064					
$\lambda_{17,4}^{(g)}$	-0.273	0.114	-0.576	0.098					

Table 8: The corretation between the latent variables ξ_1, ξ_2, and ξ_3

	$g=1$		$g=2$	
	mean	SD	mean	SD
$\rho_{12}^{(g)}$	0.64	0.02	0.71	0.02
$\rho_{13}^{(g)}$	0.08	0.03	0.01	0.03
$\rho_{23}^{(g)}$	0.06	0.03	0.08	0.03

$$\text{by } [\hat{\rho}_{ab}^{(g)}]^{(j)} = \frac{[\hat{\Phi}_{ab}^{(g)}]^{(j)}}{\sqrt{[\hat{\Phi}_{aa}^{(g)}]^{(j)}[\hat{\Phi}_{bb}^{(g)}]^{(j)}}}$$

similar ADHD symptoms in distinct genders might be totally different under collaborating with some gender related factors.

Finally, we conclude that the effects imposed by major psychiatric factor, sleep factor, and brain functional connectivity on adolescent male and female are very different even opposite. The underlying mechanism is still waiting to investigate further by introducing gender related factor about hormones and anatomical difference in brain and body.

6 Data and codes

The codes for simulation study and real data analysis, part of the data, and results are zipped and sent with this manuscript.

1. `abcd_sel.cleaned.onehot.Rds`: the cleaned real data
2. `model1.txt`: WinBUGS model file for $\mathcal{M}_1$
3. `model2.txt`: WinBUGS model file for $\mathcal{M}_2$
4. `model3.txt`: WinBUGS model file for $\mathcal{M}_3$
5. `realdata_model1_log.odc`: the result of $\mathcal{M}_1$ based on real data, for example
6. `realdata_model1_result.RData`: the result of $\mathcal{M}_1$ based on real data, for example
7. `run_model1.R`: the R codes running `model1.txt` on real data
8. `run_model2.R`: the R codes running `model2.txt` on real data
9. `run_model3.R`: the R codes running `model2.txt` on real data
10. `simData.R`: the R codes generating simulation data
11. `sim_model1.R`: the R codes running `model1.txt` on simulation data
12. `sim_model1_1_log.odc`: the result of $\mathcal{M}_1$ based on simulation data, for example

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