Dissecting individual differences in responses to naturalistic stimuli in functional MRI: effects of development and gender

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Running head: Individual differences in movie watching

Abstract

Functional MRI (fMRI) study of naturalistic conditions, e.g. movie watching, usually focuses on shared responses across subjects. However, individual differences in the responses have been attracting increasing attention in search of group differences or associations with behavioral outcomes. The individual differences have been studied by directly modeling the cross-subject correlation matrix or projecting the relations into a 1-D space. We contend that it is critical to examine whether there are single or multiple consistent components of responses underlying the whole population, because multiple components may undermine the individual relations using the previous methods. We use principal component analysis (PCA) to examine the heterogeneity of brain responses across subjects in terms of the eigenvalues of the covariance matrix, and utilize this approach to study developmental trajectories and gender effects in a movie watching dataset. We identified several brain networks in the parietal cortex that showed a significant second principal component (PC) of regional responses, which were mainly represented the younger children. The second PCs in some networks, i.e. the supramarginal network, resembled a delayed version of the first PCs for 4 seconds (2 TR), indicating delayed responses in the younger children than the older children and adults. However, no apparent gender effects were found in the first and second PCs. The analyses highlight the importance of identifying multiple consistent responses underlying individual differences in responses to naturalistic stimuli. And the PCA-based approach could be complementary to the commonly used intersubject correlation analysis.

Keywords: development; individual difference; naturalistic condition; principal component analysis; supramarginal gyrus; theory of mind; movie watching

Highlights

- There may be multiple consistent responses among subjects during movie watching
- Principal component analysis can be used to identify the multiple consistent responses
- Many brain regions showed two principal components that were separated by age
- Younger children showed delayed response in the supramarginal gyrus and precuneus

1. Introduction

Neuroimaging study of brain functions has observed a paradigm shift from using well-controlled experimental tasks or completely unconstrained resting-state to using more natural and complex stimuli such as movies and stories (Hasson et al., 2004; Nastase et al., 2019; Sonkusare et al., 2019). Compared with resting-state, naturalistic condition is more confined to the inputs, which could ensure that different subjects follow similar brain states. In contrast, the stimuli are more natural than arbitrarily defined trials and tasks, and maybe more efficient to elicit higher-order brain functions. The data analysis of naturalistic conditions usually takes advantage of the fact that there are similar brain responses across-subjects that are assumed to be induced by the common stimuli (Hasson et al., 2004). Intersubject correlations (ISC) has therefore been used to quantify the shared responses (Hasson et al., 2004; Nastase et al., 2019).

On the other hand, there are still a large amount of individual differences in responses to naturalistic stimuli. Only limited brain regions show high intersubject correlations, mostly posterior visual related regions when watching movies (Di and Biswal, 2020; Hasson et al., 2004; Nummenmaa et al., 2012). Other brain regions, such as the temporal cortex and prefrontal cortex typically showed low intersubject correlations, which may be because the functional responses in these regions are idiosyncratic across different subjects. Moreover, differences in shared responses have been shown between children and adults when watching different types of movies (Cantlon and Li, 2013; Petroni et al., 2018), in aging populations (Campbell et al., 2015), as well as in mental disorders, such as autism spectrum disorder (Byrge et al., 2015; Hasson et al., 2009; Salmi et al., 2013) and schizophrenia (Yang et al., 2019).

The analysis of individual differences in responses to naturalistic stimuli is still challenging. Until recently, some theoretical framework has been laid out to study the individual differences (Finn et al., 2020). Usually, for a given brain region (or voxel) the model of responses to naturalistic conditions are given as the following (Nastase et al., 2019):

$$x_i(t) = c(t) + id_i(t) + \varepsilon_i(t) \qquad (1)$$

where i represents the ith subject. Here c(t) represents the consistent response across subjects, id_i(t) represents the idiosyncratic response for each subject i, and ε(t) represent noises. The idiosyncratic response id_i(t) ideally is unique to each subject, therefore it is usually referred to as the source of individual differences. This is true by its definition. However, if everyone has different responses, it is difficult to link the responses to measures of group or individual differences. In a real case scenario, it is usually assumed that there is some sort of underlying canonical responses (Finn et al., 2020), which is consistent across subjects, but has different weights for each subject. The model can then be modified with an additional weighted parameter a_i:

$$x_i(t) = a_i \cdot c(t) + id_i(t) + \varepsilon_i(t) \qquad (2)$$

The estimates of a_i can then be used to be linked to group differences or individual differences. Here the model is different from Finn et al. (Finn et al., 2020), because they added the weight parameter to the idiosyncratic term *id(t)* rather than *c(t)*. But essentially the two models are the same because they both assume a canonical response that is consistent across subjects.

Given the assumption of a single canonical response, it becomes easier to link the individual differences with a group or behavioral measure. In the case of developments, we can assume some common developmental functions, e.g. Figure 1A and 1B. Function A starts to develop after a certain age with a linear increase, and reaches a plateau at a later age (Figure 1A). Function B first increases, and later decreases back. In both cases, the trends can be clearly demonstrated by using correlation matrix across-subjects (Figure 1D and 1E). However, the modeling of the relations for a continuous variable is complicated (Finn et al., 2020), especially considering the age effects as highly nonlinear. An alternative way is to project the relations into a 1-D space. A simple way is to correlate each subject's response data with the consistent component. To avoid the dependency between an individual's data and the consistent component, a leave-one-out (LOO) strategy is usually used to calculate the consistent component with the remaining subjects (Nastase et al., 2019). The individual's correlations can be used to study age effects (Figure 1G and 1H). One can also use principal component analysis (PCA) to identify the first principal component (PC), which can recover the individuals' weights simultaneously (Figure 1M and 1N).

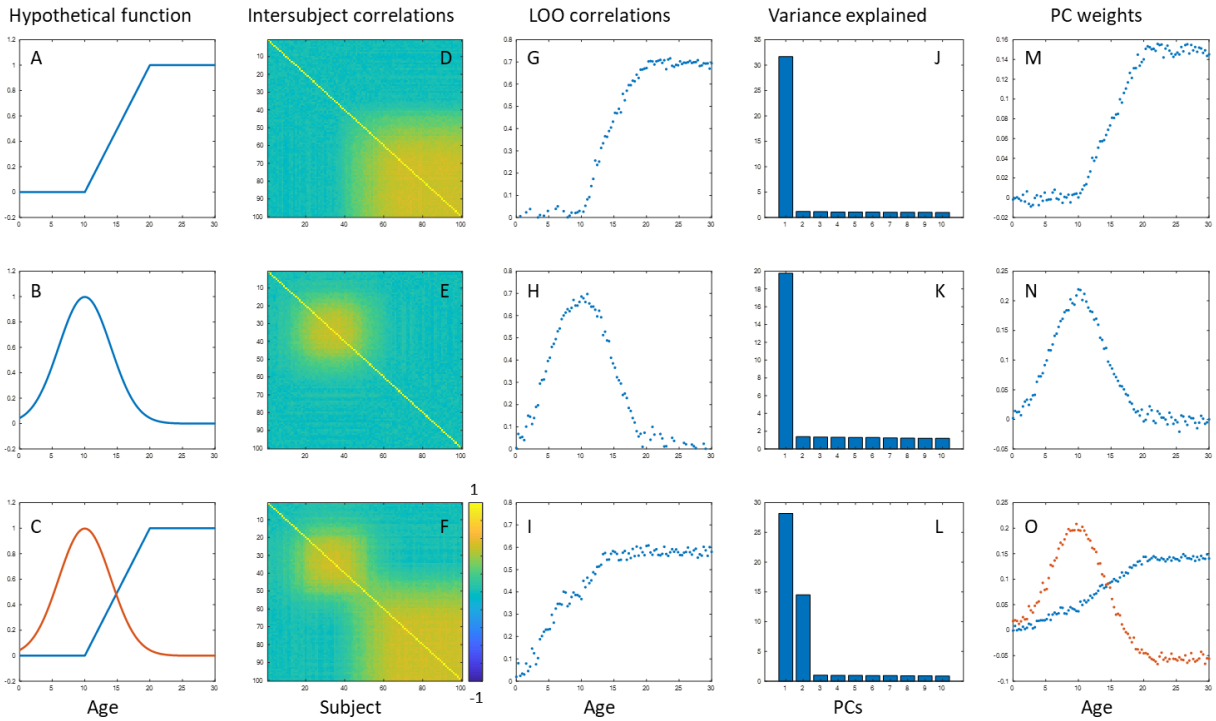

Figure 1 Illustrations of developmental effects on shared responses. A and B illustrate two hypothetical growth functions of consistent responses. The age range was set between 0 and 30 years, which overlaps with the empirical data. Note that the consistent responses in A and B may be largely different. C shows the scenario where the two separate consistent components are present in the same brain region. D through F show the correlation matrices across subjects in the three scenarios. G through I show the intersubject correlations calculated using the leave-one-out (LOO) method against the subjects' age. J through L show the percentage of variances explained by the first 10 principal components (PCs) from principal component analysis (PCA). M through O show the PC weights of the first one or two PCs against age.

So far it is assumed that there is only one canonical response, but this may not be true in real case scenario. For example, children may comprehend a cartoon movie in a different way from adults, or males and females may experience a movie very differently. If different populations have different canonical responses (e.g. Figure 1C), then the cross-subject correlations become more complicated

(Figure 1F), and it becomes difficult to recover the developmental responses using the LOO method (Figure 1I). One simple way to illustrate the presence of multiple components is to calculate the eigenvalues of the covariance matrix. As indicated by Figure 1L, two orthogonal components that can explain a large amount of variance, instead of only one in the previous cases (Figure 1J and 1K). Further, PCA can be used to recover the two different responses (Figure 1O). We argue that it is critical to examine whether there are multiple canonical responses before carrying the intersubject correlation analysis.

The study of group differences, e.g. a case-control study, also faces a similar problem. For example, we usually expect that a group of subjects with a mental disorder have lower intersubject correlations. On the other hand, all healthy subjects might have consistent responses. But the critical question becomes whether the patient group has diminished responses at all or has a different canonical responses from those in the healthy group. Again, whether there is a separate consistent response in the patient group is theoretically critical, but often overlooked in studies using LOO or similar methods.

In summary, there are intermediate positions between fully consistent responses among all the subjects and completely idiosyncratic responses for all the subjects. Different subj-groups of subjects may convey similar responses within sub-groups, but the consistent responses may vary considerably between sub-groups. We argue here that examining whether there are multiple canonical responses to naturalistic stimuli is critical in studies of individual differences in the response of naturalistic stimuli, for both continuous and categorical factors. We therefore propose a PCA-based approach to analyze fMRI data in naturalistic conditions. We analyzed a dataset of children and adults who watched an animated movie, and studied the effects of age and gender on the individual responses of the movie watching. We applied our PCA-based approach to examine whether there are multiple canonical responses present and whether the differences in responses are due to age effects or gender dimorphisms.

2. Materials and methods

2.1. Data and task

The fMRI data were obtained through openneuro (https://openneuro.org/), with accession #: ds000228. There are in total of 155 subjects, with 33 adult subjects (18 to 39 years old) and 122 children subjects (3 to 12 years old). We adopted the same criteria to remove data with poor spatial coverage and large head motion (see below) as our previous paper with only adult subjects analyzed (Di and Biswal, 2020). As a result, 82 subjects were included in the current analysis (29 adults and 53 children subjects). There are 45 females and 37 males. The original study was approved by the Committee on the Use of Humans as Experimental Subjects (COUHES) at the Massachusetts Institute of Technology.

During the fMRI scan, the subjects watched a silent version of Pixar animated movie "Partly Cloudy", which is 5.6 minutes long (https://www.pixar.com/partly-cloudy#partly-cloudy-1). Brain MRI images were acquired on a 3-Tesla Siemens Tim Trio scanner using the standard Siemens 32-channel head coil. Functional images were collected with a gradient-echo EPI sequence sensitive to BOLD contrast in 32 interleaved near-axial slices (EPI factor: 64; TR: 2 s, TE: 30 ms, flip angle: 90°). The voxel size was 3.13 mm isotropic, with 3 subjects with no slice gap and 26 subjects with a 10% slice gap. 168 functional images were acquired for each subject, with four dummy scans collected before the real scans to allow for steady-state magnetization. T1-weighted structural images were collected in 176 interleaved sagittal slices with 1 mm isotropic voxels (GRAPPA parallel imaging, acceleration factor of 3; FOV: 256 mm). For more information for the dataset please refers to (Richardson et al., 2018).

2.2. FMRI data analysis

2.2.1. Preprocessing

FMRI data processing and analyses were performed using SPM12 and MATLAB (R2017b) scripts. A subject's T1 weighted structural image was first segmented into gray matter, white matter, cerebrospinal fluid, and other tissue types, and was normalized into standard Montreal Neurological Institute (MNI) space. The T1 images were then skull stripped based on the segmentation results. Next, all the functional images of a subject were realigned to the first image of the session and coregistered to the skull stripped T1 image of the same subject. Framewise displacement was calculated for the translation and rotation

directions for each subject (Di and Biswal, 2015). Subjects who had maximum framewise displacement greater than 1.5 mm or 1.5^{o} were discarded from further analysis. The functional images were then normalized to MNI space using the parameters obtained from the segmentation step with a resampled voxel size of 3 x 3 x 3 mm^3. The functional images were then spatially smoothed using a Gaussian kernel of 8 mm. Lastly, a voxel-wise general linear model (GLM) was built for each subject to model head motion effects (Friston's 24-parameter model) (Friston et al., 1996), low-frequency drift (1/128 Hz), and constant offset. The residuals of the GLM were saved as a 4-D image series, which were used for further intersubject correlation analysis.

We used the same head motion threshold as our previous study (Di and Biswal, 2020). We calculated framewise displacement in translation and rotation separately (Di and Biswal, 2015), and removed subjects with maximum framewise displacement greater than 1.5 mm or 1.5^{o}. As a result, 82 subjects were included in the final analysis.

2.2.2 Independent component analysis

We performed the proposed analysis on two spatial scales. Firstly, we did it on a small number of large-scale networks. This enabled us to perform an in-depth analysis of the time courses to investigate developmental and gender effects. Secondly, we performed a voxel-wise analysis to demonstrate spatial distributions of the effects. For the first aim, we performed spatial independent component analysis (ICA) to define large-scale networks using Group ICA of fMRI Toolbox (GIFT) (Calhoun et al., 2001). Twenty components were extracted. The resulting IC maps were visually inspected, and fifteen maps were included in the subsequent analysis as functionally meaningful brain networks. The ICs were grouped into three groups for illustration purposes according to their spatial locations (Figure 2). The full maps of all the 20 ICs can be found at: https://neurovault.org/collections/INSJUAIW/. A time series was back-reconstructed to each subject for each IC using group ICA method. The time series were z transformed, and used for further intersubject analysis. To avoid confusion with PCA in the current paper, we refer to the IC maps as networks below.

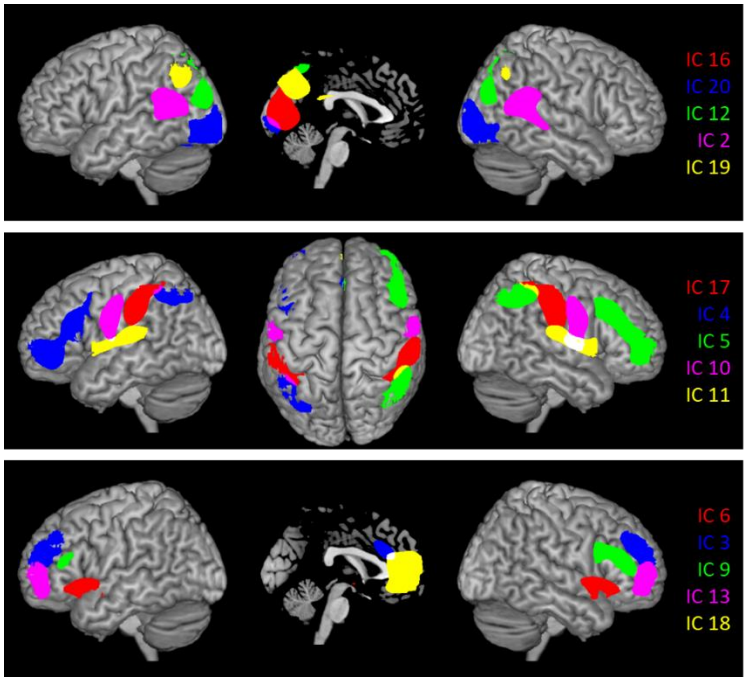

Figure 2 Maps of independent components (ICs) included in the current analysis. The maps were grouped based on their spatial locations. Top row, visual related networks; middle row, frontoparietal networks; bottom row, frontal and insular networks. The maps were thresholded at z > 2.3 after spatially z-transformed.

2.2.3. Principal component analysis

For each network (IC), we performed PCA on a 168 (time points) x 82 (subject) matrix *X*. The goal of the PCA is to identify whether one or more components can explain the temporal fluctuations in response to the movie stimuli among all the subjects. PCA identifies a transformation matrix *W* (82 x 82) to transform the individual response matrix *X* into a series of principal components *T* (168 x 82). The transformation can be written as:

$$T = X \cdot W \qquad (3)$$

T represents 82 vectors of PCs. The variance explained by each PC is indexed by the eigenvalue of the covariance matrix of *X*. The percentage variance explained by each PC can then be calculated by the

eigenvalue of that PC over the sum of eigenvalues of all the PCs. If there is only one canonical response among all the subjects, the first PC should explain a large amount of variance, but later PCs should explain very low variances that reflect noises. The variance explained by the first PC could be a similar measure as the overall intersubject correlation across subjects. However, if there is more than one canonical response, the later PCs may also explain a large portion of the variance.

We are only interested in a few PCs. For a specific component i, the transformation can be expressed as a simpler form:

$$t_i = X \cdot w_i \qquad (4)$$

The ith component t_i (a.k.a. the PC score) can be seen as a consistent response. And the weight vector w_i is the weight of each subject on the consistent response, which can represent a_i in equation 2. PC loadings are the PC weights multiplying the standard deviation of the eigenvalue, which can reflect the relative importance of each PC.

Specifically, we performed PCA in MATLAB by using the singular value decomposition algorithm. It is noteworthy that the input 82 time series were already z transformed. To determine whether a PC explained greater than the random level of variance, we performed a permutation test with 10,000 permutations for each network. For each permutation, the temporal order of time series of each subject was shuffled, and PCA was performed. The variance explained by the first PC was obtained. The distribution of variance explained by the first PC across the 10,000 permutations was used to determine the statistical significance level. Here, we used 99.9 percentile ($p < 0.001$) as a threshold. These thresholds were very similar for all the 15 networks. Therefore, we averaged the thresholds to obtain a finale threshold. The PCs with variance explained larger than the threshold were considered non-random PCs.

2.2.4. Age and gender effects

After obtaining multiple PCs for a network, one important question is whether a given factor of interest differentiate the PCs, in the current case age and gender. If different ages or genders are represented

differently in the PCs, then it suggests that there are multiple canonical responses in different age or gender groups. For developmental effects, we fitted the PC loading vector with different developmental functions.

Model 1, baseline: $y = \beta_0 + \varepsilon$

Model 2, linear age: $y = \beta_0 + \beta_1 \cdot age + \varepsilon$

Model 3, quadratic age: $y = \beta_0 + \beta_1 \cdot age + \beta_2 \cdot age^2 + \varepsilon$

Model 4, quadratic log age: $y = \beta_0 + \beta_1 \cdot \log(age) + \beta_2 \cdot \log(age)^2 + \varepsilon$

Model 5, exponential age: $y = \beta_0 \cdot (1 - e^{-\beta_1 \cdot (age + \beta_2)}) + \varepsilon$

Model 1 represents a baseline model without any age effects. Model 2 and 3 represent linear and quadratic age effects. Model 4 represents similar quadratic age effects but with logarithmic age to account for the asymmetry of increasing and decreasing during developments. And the last exponential model represents a plateau model, where the development reaches a plateau after a certain age. The models were fitted using scripts in MATLAB. After model estimation, Akaike information criterion (AIC) was used to compare the evidences of all the models. And the model with the best evidence was selected. The first PCs were compared for all the 15 networks. And the second PCs were only compared for the 10 networks with significant variance explained than random.

For the gender effects, we performed a two-sample t-test between males and females for each PC and network. The first PCs were compared for all the 15 networks. And the second PCs were only compared for the 10 networks with significant variance explained than random.

2.2.5. Behavioral correlates

Lastly, we asked whether the two PCs of different networks can provide complementary information in explaining the variability of a behavioral measure. Test scores of theory of mind performance are available for the children subjects (n = 53). The theory of mind battery includes custom-made stories and questions that require an understanding of the characters' mental states. The theory of mind task

performance was summarized as the proportion of correct questions out of the 24 items. More information about the task and scores can be found at Richardson et al. (2018). For each network, we built regression models to explain the variance of theory of mind performance using the PC loadings of either of the PCs or the combination of the two PCs. For the first two models, we used F statistics to identify significance compared with a reduced model with only constant. For the third model, we considered the t statistics of the two PC regressors to identify the network with both PCs having significant unique contributions.

2.2.6. Voxel-wise variance maps

Lastly, we performed voxel-wise PCA to show the spatial distributions of the first and second PC effects. For each voxel, PCA was performed on a 168 x 82 matrix after each column was z transformed. The percentage of variance for the first and second PCs were obtained for each voxel, thus forming two spatial maps.

3. Results

3.1. Principal component analysis

To examine whether there are multiple canonical responses present, we performed PCA on the 15 networks and obtained the percentage of variances explained by the PCs (Figure 3 shows the first three PCs). The variance explained by the first PC represents how a single canonical response accounts for the variance of all the subjects, which is similar to a conventional intersubject correlation. For a few networks, the first PC explained a large amount of variance, e.g. larger than 15% of the total variance. Among the six, five were visual related networks and the remaining one (IC 17) was the supramarginal gyrus region. These are consistent with our previous voxel-wise analysis in only adult subjects (Di and Biswal, 2020). The second or later PCs are more interesting, because they may suggest multiple canonical responses. In the current case, 10 out of 15 networks explained greater than chance level

variances. Notably, the second PC of the supramarginal gyrus network (IC17) explained more than 6% of the variance. Other networks included the superior visual network (IC12) and the precuneus network (IC19). For one network (IC4), the third PC also explained above chance variance, but all the first three PCs explained relatively fewer variances compared with other networks. It is noteworthy that the variance explained by the second PC would be much less than those explained by the first one. But it may be still meaningful, the differences in variance explained may reflect the number of subjects represented in each group.

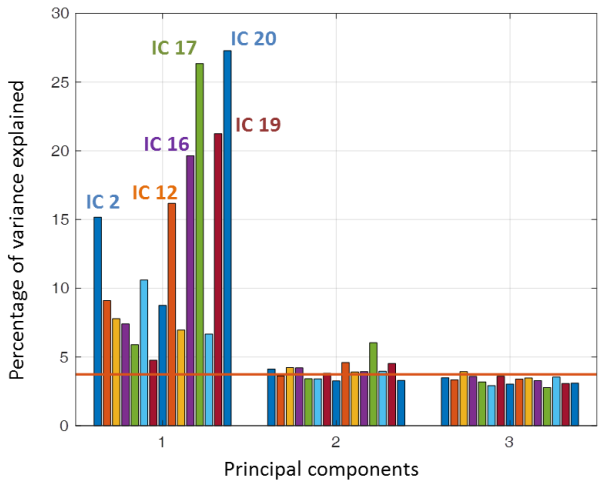

Figure 3 Percentage of variance explained by the first three principal components of each of the 15 networks (independent components, IC). The horizontal line indicates 99.9 percentile of chance level ($p < 0.001$) by using permutation tests.

We focus on the networks whose first two PCs both explained a relatively large amount of variances. The first example is the supramarginal gyrus network (IC17) whose first PC explained the second large amount of variance among the first PCs of all the networks, and the second PC explained the most variance among the second PCs of all the networks. The correlation matrix across subjects showed that older subjects had greater intersubject correlations, and the subjects #10 through #20 seemed to have very weak or no correlation with order subjects (Figure 4A). The loadings of the first PC were mostly

positive, and there seemed a trend of higher loadings for adult subjects. In contrast, the loadings of the second PC were mostly represented by young children, and some adult subjects showed small negative loadings. No clear gender differences can be found in both of the PCs. Most interestingly, the time courses of the two PC scores looked similar, but the second PC was delayed compared with the first PC (Figure 4D). Cross-correlation analysis confirmed 2-TR (4 s) delays between the two PCs (Figure 4E).

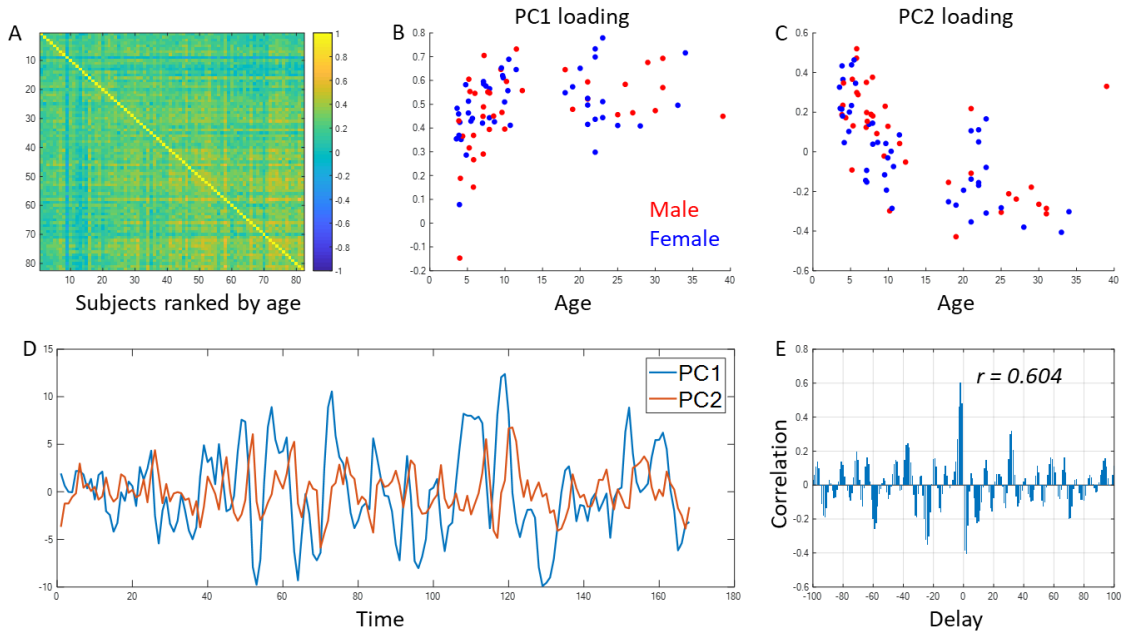

Figure 4 The first two principal components (PCs) of the supramarginal gyrus network (independent component 17). A, Correlation matrix across the 82 subjects, where the subjects were sorted by their age. B and C, PC loadings for the first (B) and second (C) PCs against age. The colors of the dots reflect the subjects' gender. D, PC scores of the two PCs. E, cross-correlations between the first and second PCs.

We also explored the other networks. In the supplementary materials, we show two other examples of the precuneus network (IC19) and the superior visual network (IC12). We observed similar PC loadings trends as the supramarginal network. Both the first PCs showed a maturation curve, and the second PCs showed high loadings for younger children. The second PC of the precuneus network was also a delayed version of the first PC (Figure S1). However, the first two PCs of the superior visual

network (IC12) did not show high cross-correlations (Figure S2). The cross-correlations were further examined in the medial visual network (IC16) and temporoparietal junction network (IC2), which also showed low cross-correlations (Figure 5).

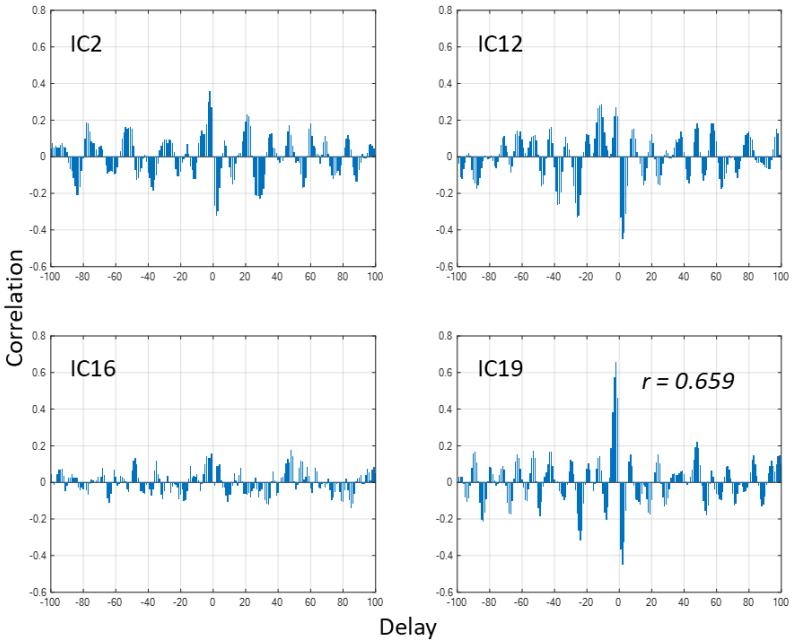

Figure 5 Cross correlations for four networks (independent component, IC). IC2, temporoparietal junction network; IC12, superior visual network; IC16, medial visual network; and IC19, precuneus network.

3.2. Developmental trajectories

For the first PCs of all the 15 networks, the PC loadings showed some kinds of maturation curves. 12 networks fitted well with the exponential model (Figure 6A and 6B), and the three remaining networks fitted well with the quadratic log age model (Figure 6C). For the exponential developmental functions, we calculated the age when the developmental curve reached 90% of the total response. The 90% development ages ranged from 4.88 years (frontal pole network, IC13) to 14.52 years (lateral visual

network, IC20). For the quadratic log age models, we calculated the age at peak, which ranged from 8.73 years (left frontoparietal network, IC4) to 10.34 years (paracentral network, IC10).

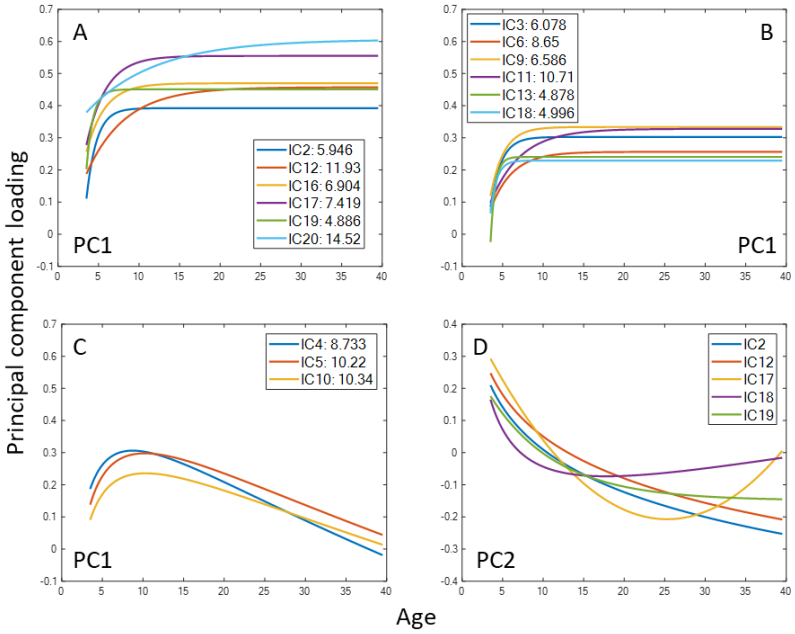

Figure 6 Fitted developmental trajectories of principal component (PC) loadings of the first (A, B, and C) and second PCs (D). In A and B, the numbers following each IC # indicate the age when the developmental curve reached 90% of the total response; and in C, the numbers indicate the age at peak.

The second PCs of five networks showed higher weight at the earliest age (Figure 6D). This suggests that these PCs and their corresponding first PCs represented responses in different age groups. The second PCs of the remaining networks are shown in the supplementary Figure S3, which showed a variety of trends.

3.3. Gender effects

In contrast to the developmental effects, there were no clear gender effects for the first PCs of all the 15 networks (Figure 7). No networks showed statistically significant differences between males and females in the two-sample t-tests (all $p > 0.05$). For the second PCs of the ten networks tested, one network

showed significant gender effects at $p < 0.05$ (IC2: $p = 0.024$), which could not survive multiple comparison correction.

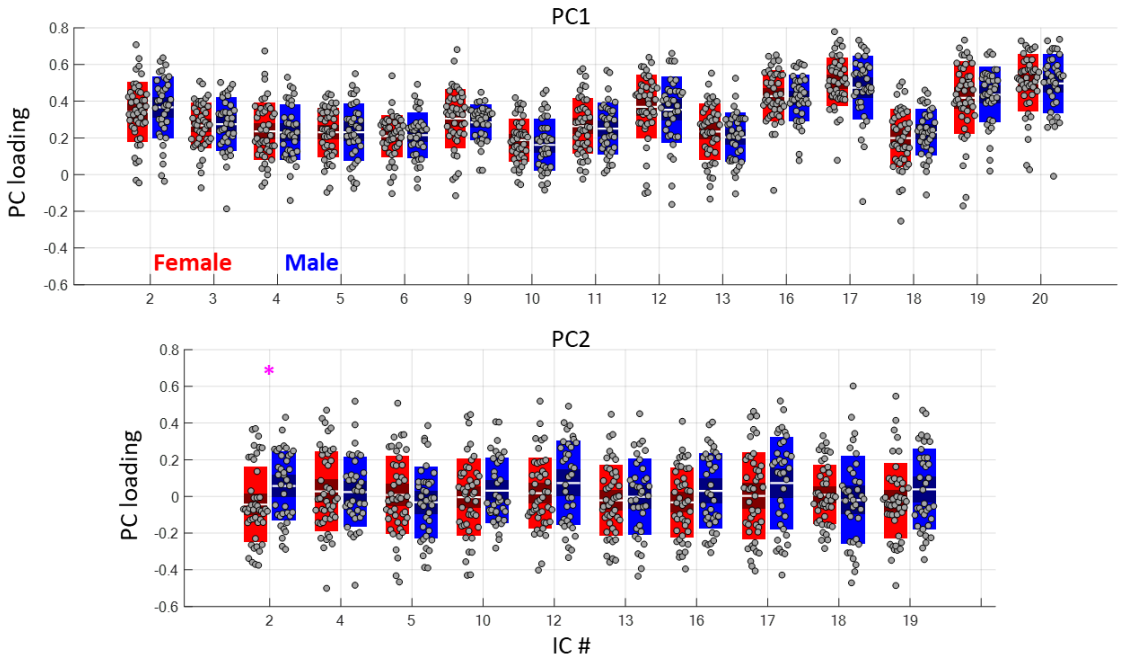

Figure 7 Gender effects on the principal component (PC) loadings of the first and second PCs in the 15 networks (independent components, IC). The asterisk indicates statistically significant at $p < 0.05$. The plots were made by using notBoxPlot (https://github.com/raacampbell/notBoxPlot).

3.4. Correlations with theory of mind performance

We asked whether the two PCs of different networks can provide complementary information in explaining the variations of theory of mind task performance (proportion correct). For each network, we built regression models with the PC loadings from only one of the PCs or the combination of the two together (Figure 8). For the first PC, the supramarginal network (IC17) had the highest correlation with theory of mind performance, following with the insula cortex network (IC6), the visual cortex network (IC16), and the lateral frontal cortex (IC9). However, including the second PC in these networks did not increase the variance explained much. On the other hand, although the first PC of the temporoparietal

junction network (IC2) had a relatively small correlation with theory of mind performance, combining the two PCs had significantly the variance explained.

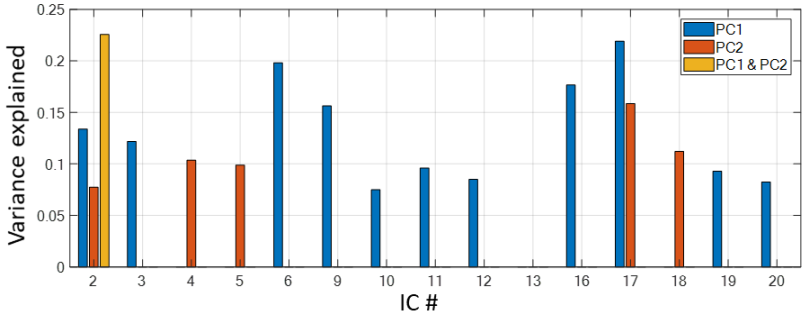

Figure 8 Explaining the variance of theory of mind performance by using the first two principal component (PC) loadings in the 15 brain networks (independent components, IC). The regression models were built using the first and second PC alone (blue and red bars), and with the two PCs together (orange bars). The blue and red bars are only shown when the model was $p < 0.05$ in the f-test. The orange bars are only shown when $p < 0.05$ in the t-tests of both of the regressors.

3.5. Voxel-wise variance maps

Lastly, we calculated percentage variance maps that are explained by the first and second PCs (Figure 9). Not surprisingly, the variance explained by the fist PCs resembled the intersubject correlation map reported previously (Di and Biswal, 2020), which only included adult subjects. It should be noted that the percent variance explained by the first PC is always larger than the second PC. Therefore, different thresholds were used. But it can be seen that most of the high variance regions by the second PC overlapped with those of the first PC, but with some exceptions. Firstly, the medial occipital regions did not have high variance explained by the second PCs. Secondly, regions in the parietal lobe showed relatively larger variance explained by the second PCs, while their first PCs explained less than 9% of the variance (see also supplementary Figure S4).

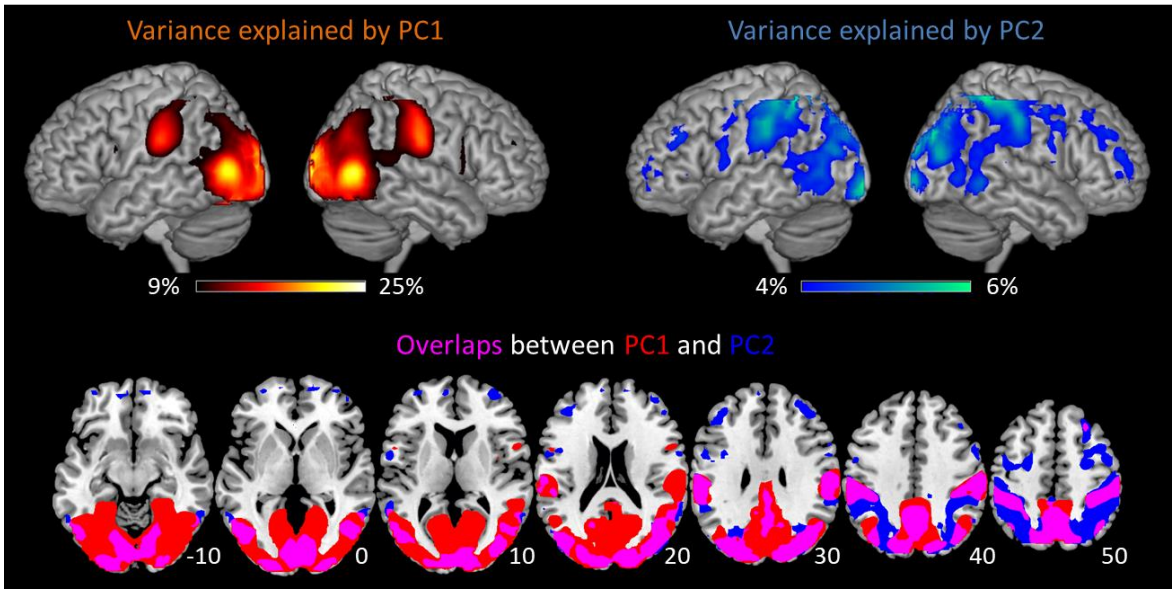

Figure 9 Maps of variances explained by the first (top left) and second (top right) principal components (PCs) in each voxel. The maps were arbitrarily thresholded at 9% and 4% of variances for the first and second PCs, respectively. The overlaps between the variance maps of the two PCs are shown at the bottom. The numbers near each slice represent z coordinates in Montreal Neurological Institute (MNI) space. The unthresholded maps can be found at: https://neurovault.org/collections/INSJUAIW/.

4. Discussion

In the current paper, we proposed a PCA-based analysis framework to study individual differences in response to naturalistic stimuli in fMRI data, to examine the possibility of the existence of multiple canonical responses in different sub-groups. On a movie watching dataset of children and adults, we showed that for many regions there was a second PC that may represent a second canonical response to the movie. The first and second PCs were not separated by gender, but by age distributions, suggesting that the kids around 5 years old had a very different response pattern than the older subjects. Interestingly, in several regions, e.g. the supramarginal gyrus and the precuneus, the second PC represented delayed responses than the first PC for 4 seconds (2 TR). Besides, we showed that the two PCs in some regions,

e.g. temporoparietal junction, conveyed complementary information to explain the variance of theory of mind performance. Lastly, the voxel-wise analysis highlighted the superior parietal regions that had high variance explained by the second PC while relatively low variance was explained by the first PC.

By calculating the eigenvalues and variance explained by different PCs, we first provided evidence that many brain networks and regions might possess two different patterns of responses to the movie stimuli. In terms of networks, the supramarginal network (IC17), the precuneus network (IC19), and the superior visual network (IC12) had the highest variance explained by the second PCs. This has been confirmed by the voxel-wise analysis. The first and second PCs of each of these networks were not separated by gender, but by their developmental trajectories, indicating fundamentally different responses in younger and older subjects in this sample. Without using the PCA based analysis, the responses of the second PC would be overlooked. It is noteworthy that although the variance explained by the second PCs were much smaller than those by the first PCs, the smaller variance may reflect the fact that there are fewer subjects in the very young group but not the functional significance of the second PCs.

What are the differences between the first and second PCs in these networks? For some of the networks, e.g. the supramarginal network (IC17）and the precuneus network (IC19), the second PC seemed to be a delayed version of the first PC with a delay of 4 seconds. This suggests that younger subjects had a delayed response as their older counterparts when watching the movie. These regions are responsible for theory of mind (Silani et al., 2013) and higher-order presentations and memory (Carhart-Harris and Friston, 2010; Chen et al., 2017). It may reflect the fact that the understanding of the movie in younger subjects is slower. However, an alternative explanation exists that the delayed responses may due to the delay of hemodynamic response rather than the delay of underlying neural activity. It is possible because there is some evidence of differences in hemodynamic responses functions between children and older subjects (Jacobs et al., 2008). There are still no systematic examinations of hemodynamic response delays in children, which need to be further explored. It is also noteworthy that for other networks the second PC may not simply be a delay version of the first PC, e.g. the superior

visual network (IC12), because their cross-correlation did not show high values at the delay of 2 TR. However, visual inspection suggests that there may still be delays between the two PCs, but the delays may not be constant across time (Figure S2). All the data suggested that the differences in responses in younger and older subjects may not be simply quantified as differences in response strength or delays. More complicated models may be needed to fully understand the differences between young and older subjects.

One limitation of PCA is that the interpretation of different PCs is not straightforward. For the current analysis, although the first and second PCs showed loading distribution differences in age, the two PCs do not directly represent the averaged responses of two age groups. The second PC represents some differences in the temporal features of the responses across the whole sample. For this reason, the loadings of the second PC were not completely zeros for the older subjects but with negative weights (Figure 4C and 6D). In addition, considering the autocorrelations of blood-oxygen-level dependent (BOLD) signals (Friston et al., 1994), two time series with a 4-s delay will not show complete zero correlations. But the PCA algorithm forces the second PC to be orthogonal to the first PC. This will also make the second PC not exactly represent the responses in the children subjects. Some other methods may be used to directly show the responses in the children group.

The temporoparietal junction plays an important role in theory of mind and the understanding of social interactions (Samson et al., 2004; Saxe and Kanwisher, 2003). In the current analysis, the first PC of the temporoparietal junction network (IC2) explained more than 15% of the variance, and the second PC also explained greater than random variance. Most importantly, the first and second PCs of this network conveyed complementary information to the theory of mind performance measures. This suggests that the neural activity underlying theory of mind may be complex in the temporal domain. And only considering the amplitude of responses across subjects cannot fully capture the neural dynamics underlying the individual differences. Another interesting finding of this network is that the loadings of the second PC showed gender effect. It should be noted that these effects were not statistically significant

after multiple comparisons, suggesting they may be a false positive. However, these results do suggest potential interesting effects that warrant further studies.

The PCA-based method is promising to study movie watching data compared with the conventional correlation-based method. The eigenvalues of the covariance matrix can provide critical information about potential multiple canonical responses. Even in case of only one canonical response, the PCA-based method can still provide equivalent information as intersubject correlations. The eigenvalue and variance explained by the first PC is a similar measure as averaged intersubject correlations. Moreover, the loadings of the first PC provide a simple way to project the consistent response to an individual's space, which is easier than correlating each subject's time series with the overall averaged time series or using the LOO method (Nastase et al., 2019). Therefore, the PCA-based approach can be an alternative way to analyze movie watching data.

There are a few limitations to the current study. First, we separately examined the developmental and gender effects of the shared responses, however, developmental and gender effects may interact with each other. Further studies may examine the developmental trajectories separately for males and females to verify whether gender moderates the developmental trajectories, which require larger sample sizes for each group. Secondly, studies have shown that the shared responses are dynamic (Di and Biswal, 2020; Simony et al., 2016). The presence of multiple response components may also be sensitive to the movie context, thus showing fluctuations. Further studies may take dynamics into account to fully characterize the developmental trajectories.

5. Conclusion

In the current study, we proposed a PCA-based approach to analyze individual differences in response to naturalistic stimuli. With an example of children and young adult dataset, we showed that young children had a very different pattern of responses than older children and adults, which in many brain regions

showed delayed responses. The results highlight the importance of identifying multiple consistent components when studying shared responses to naturalistic stimuli.

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Conflict of interest

The authors declared that there is no conflict of interest.

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