A spatio-temporal atlas of the growing brain for fMRI studies

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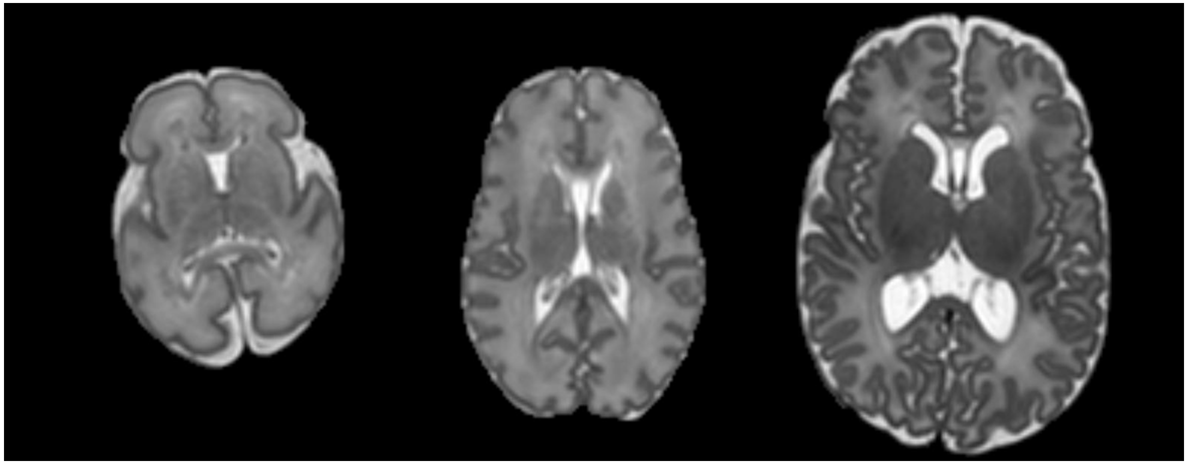
Outline

- Motivation
- Average models of brain and brain growth
- B-spline transformations for modeling average brain growth
- Anatomical template of the growing brain
- Visualising development of brain networks from resting state fMRI
- Conclusion

Motivation

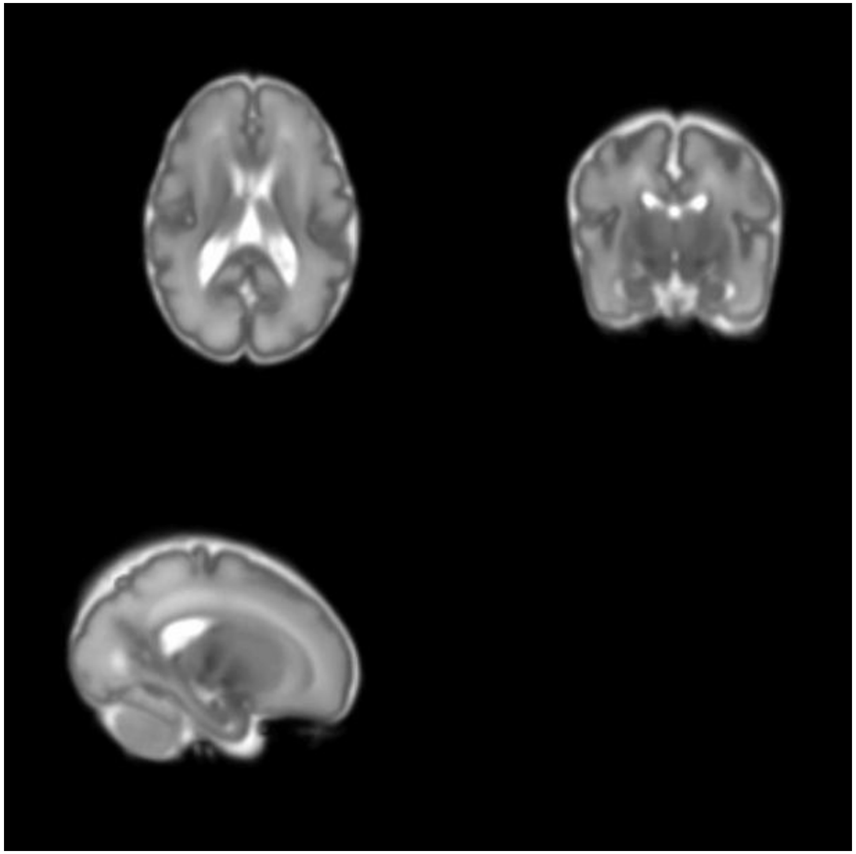
- The aim: to understand brain development during the 3rd trimester of pregnancy
- Specifically: development of activation maps such as default mode and motor network
- Challenge: data scattered across different subjects and ages



29 weeks GA   35 weeks GA   42 weeks GA

4D model of average growth

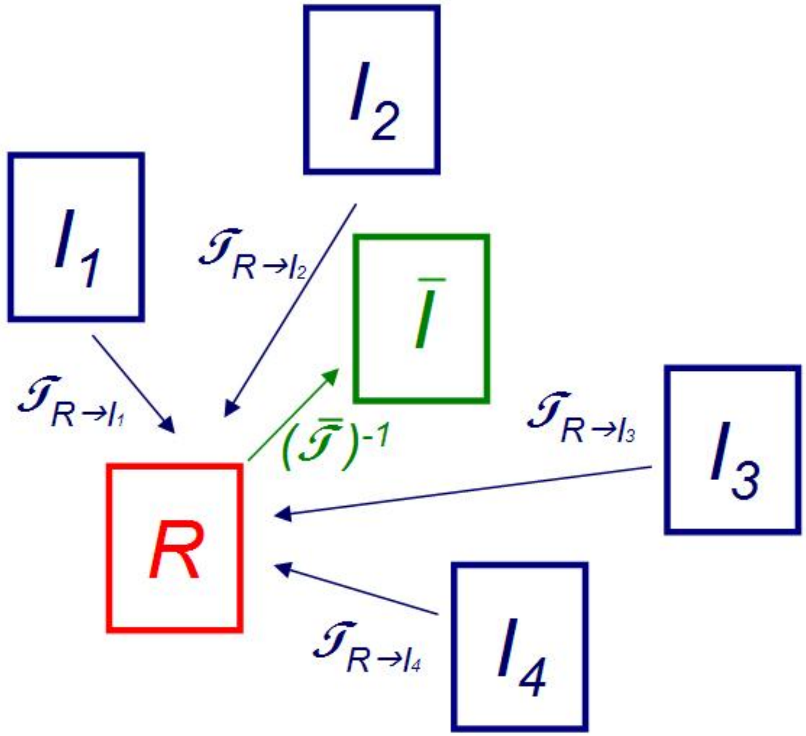
- The aim:
  - to construct average 4D spatio-temporal model of growing brain (3D for brain anatomy + 1D for age)
- Solution:
  1. Construct the average anatomy of growing brain
  2. Create average model from additional information attached to the anatomy



Non-rigid template
B-spline registration 2.5 mm
(103 images 28-44 weeks GA)

Average models of brain (3D)

- To visualise average brain anatomy
- Training images are registered to a reference subject
- Inverse of the average transformation is used to find the average brain space
- Training images are transformed to the average space and their intensities averaged

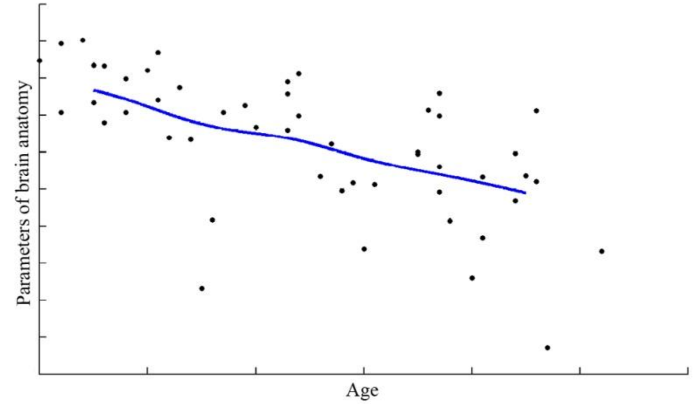


$$\bar{\mathcal{T}} = \frac{1}{n}\sum_{k=1}^{n} \mathcal{T}_{R\rightarrow I_k}$$

Average models of brain growth (4D)

- To calculate age-dependent average anatomical templates, average transformation is replaced by age-dependent weighted average:

$$\bar{\mathcal{T}}(t) = \frac{\sum_{k=1}^{n} w(t_k, t)\mathcal{T}_{R\to I_k}}{\sum_{k=1}^{n} w(t_k, t)}$$



$$w(t_k, t) = \frac{1}{\sigma\sqrt{2\pi}} \exp^{\frac{-(t_k - t)^2}{2\sigma^2}}$$

Age of the subject (t_k)

Age for the template (t)

Template for the age *t*

$$\bar{I}(t) = \frac{\sum_{k=1}^{n} w(t_k, t) I_k \circ \mathcal{T}_{R\to I_k} \circ \bar{\mathcal{T}}^{-1}(t)}{\sum_{i=1}^{n} w(t_k, t)}$$

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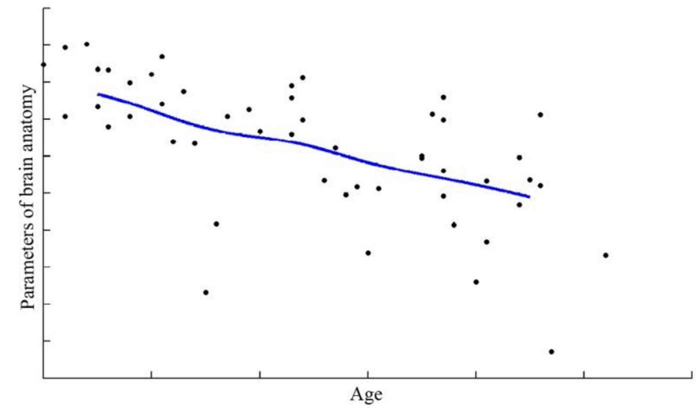

$$w(t_k, t) = \frac{1}{\sigma\sqrt{2\pi}} \exp^{\frac{-(t_k - t)^2}{2\sigma^2}}$$

Age of the subject (t_k)

Age for the template (t)

Template for the age *t*

Registration? ($\mathcal{T}_{R\rightarrow I_k}$)

$$\bar{I}(t) = \frac{\sum_{k=1}^{n} w(t_k, t) I_k \circ \mathcal{T}_{R\rightarrow I_k} \circ \bar{\mathcal{T}}^{-1}(t)}{\sum_{i=1}^{n} w(t_k, t)}$$

Average models of brain growth (4D)

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$$\bar{\mathcal{T}}(t) = \frac{\sum_{k=1}^{n} w(t_k,t)\mathcal{T}_{R\rightarrow I_k}}{\sum_{k=1}^{n} w(t_k,t)}$$

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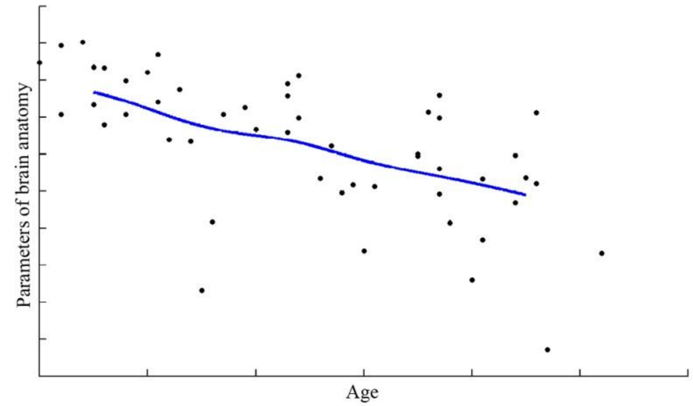


Age for the template

Age of the subject

Template for the age *t*

Registration?

Averaging transformations?

$$\bar{I}(t) = \frac{\sum_{k=1}^{n} w(t_k,t) I_k \circ \mathcal{T}_{R\rightarrow I_k} \circ \bar{\mathcal{T}}^{-1}(t)}{\sum_{i=1}^{n} w(t_k,t)}$$

Registration

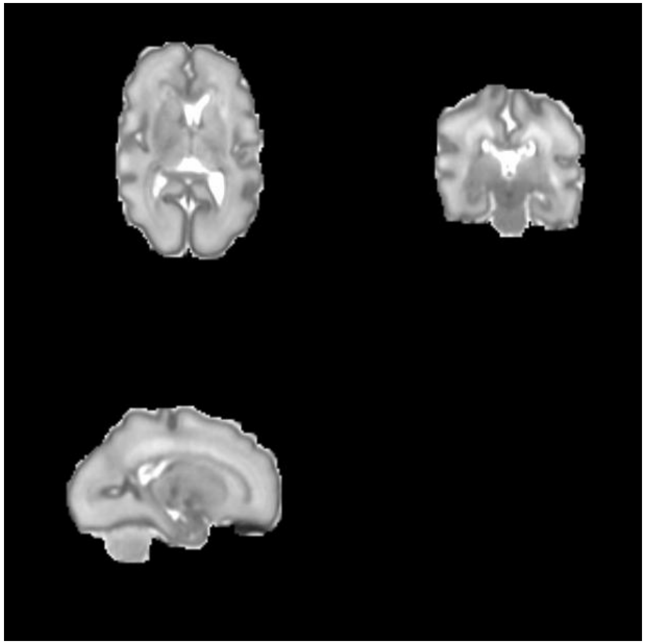
- We used B-spline FFD registration (Rueckert *et al.* 1999)
- Transformation model:

$$T(v) = A(v) + B(v)$$

Global affine component: 12 parameters (translation, rotation, scaling and skewing)

Local component – B-spline

- Similarity measure:
  - Normalised mutual information (NMI)
  - Challenge: NMI too weak – boundaries of the brain not always aligned correctly
  - Solution: removing extra-cranial CSF



Longitudal registration: subject at 30, 34 and 40 weeks GA

Model for the transformation

- Global shape change is not important when assessing the development of activation network => images are affinely aligned in pre-processing step
- We model only local shape change using B-spline transformation:

Basis functions

$$T(v) = \sum_i B_i N_i(v)$$

Control points

- All transformations are defined on the same lattice in the space of the reference image

Averaging B-spline transformations

- We assume small deformation setting
- Transformations defined on the same lattice

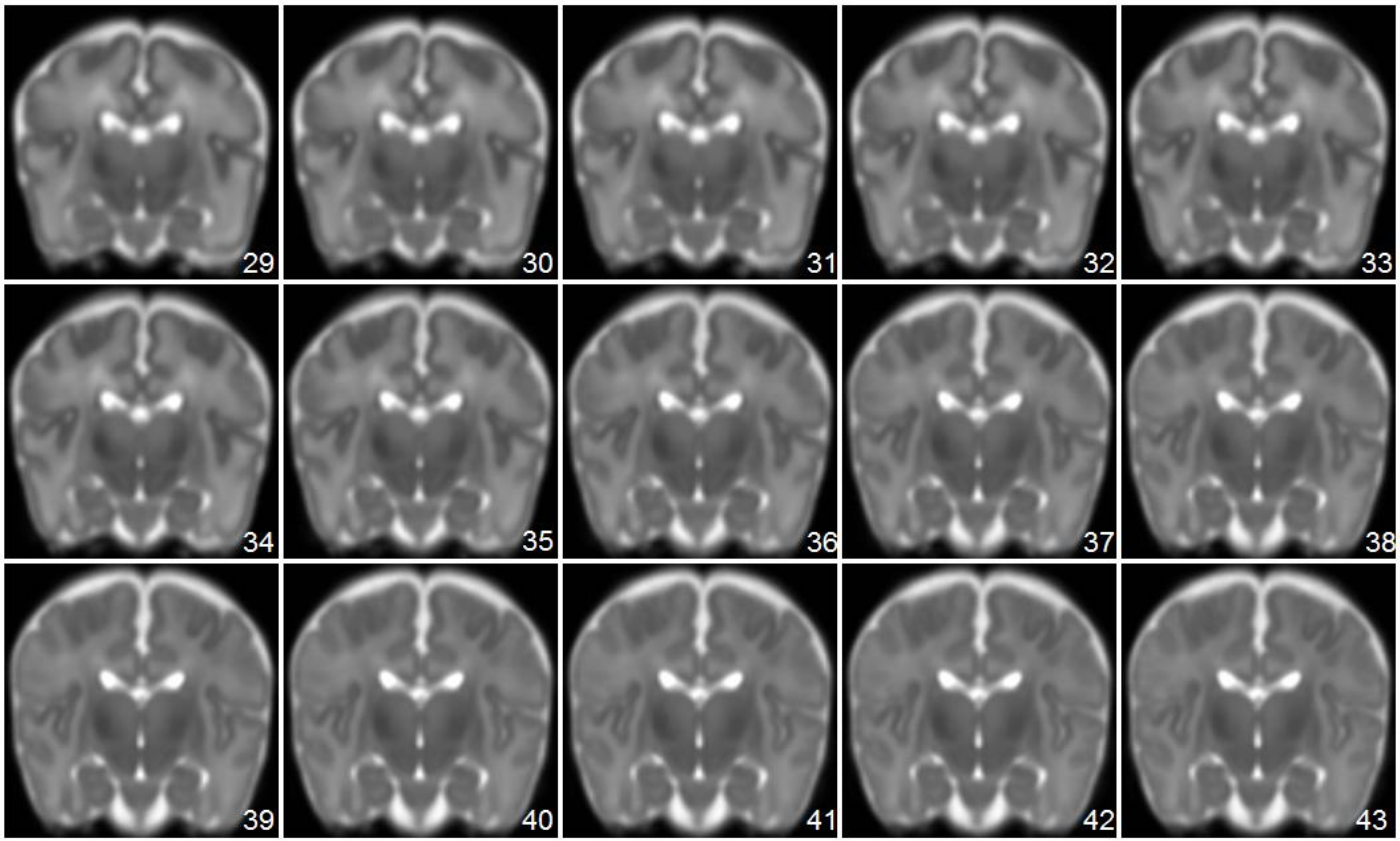
  => the averaging of B-spline transformations can be approximated by averaging the control points:

$$\bar{T}(v) = \sum_i \bar{B}_i N_i(v), \ \bar{B}_i = \frac{1}{n}\sum_{k=1}^{n} B_{i,k}$$

- Inverse transformation is not a B-spline, but can be numerically approximated as a B-spline

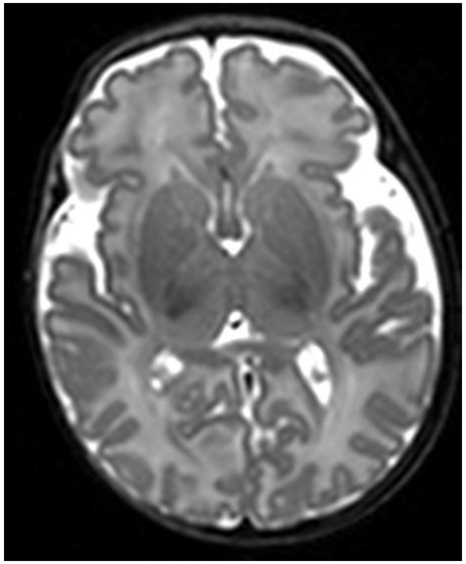
Anatomical template of growing brain

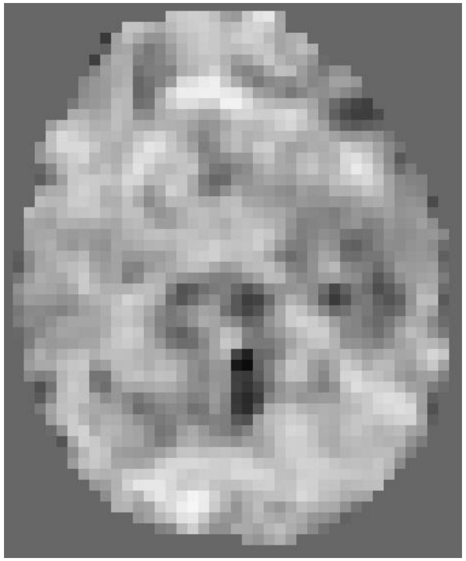
- Created using 103 T2-weighted MR images of premature babies with ages 28-44 weeks GA
- B-spline control point spacing 5mm
- Standard deviation 2 weeks for calculating weights



fMRI data

- 39 subjects (29-44 weeks GA) consisting of anatomical template and aligned resting-state fMRI data
- Correlation maps were estimated from fMRI data by placing the seed in left motor cortex/medial prefrontal cortex and calculating correlation of time-series with the rest of the brain using FSL





Creating average activation maps

- The 4D anatomical template has been created
- Only 39 fMRI datasets =>we chose to use average template from 103 images as a basis for the model
- The anatomical images with the attached correlation maps can now be registered to the average anatomical template to create average 4D correlation maps

Creating average activation maps

- 39 anatomical images were registered to the average template of corresponding age
- Corresponding correlation maps were then transferred not only to the corresponding template but also to neighbouring frames=>smooth model
- Average time-depended correlation maps were obtained by weigted averaging at each time-point

Average correlation map at time-point *t*

Correlation map

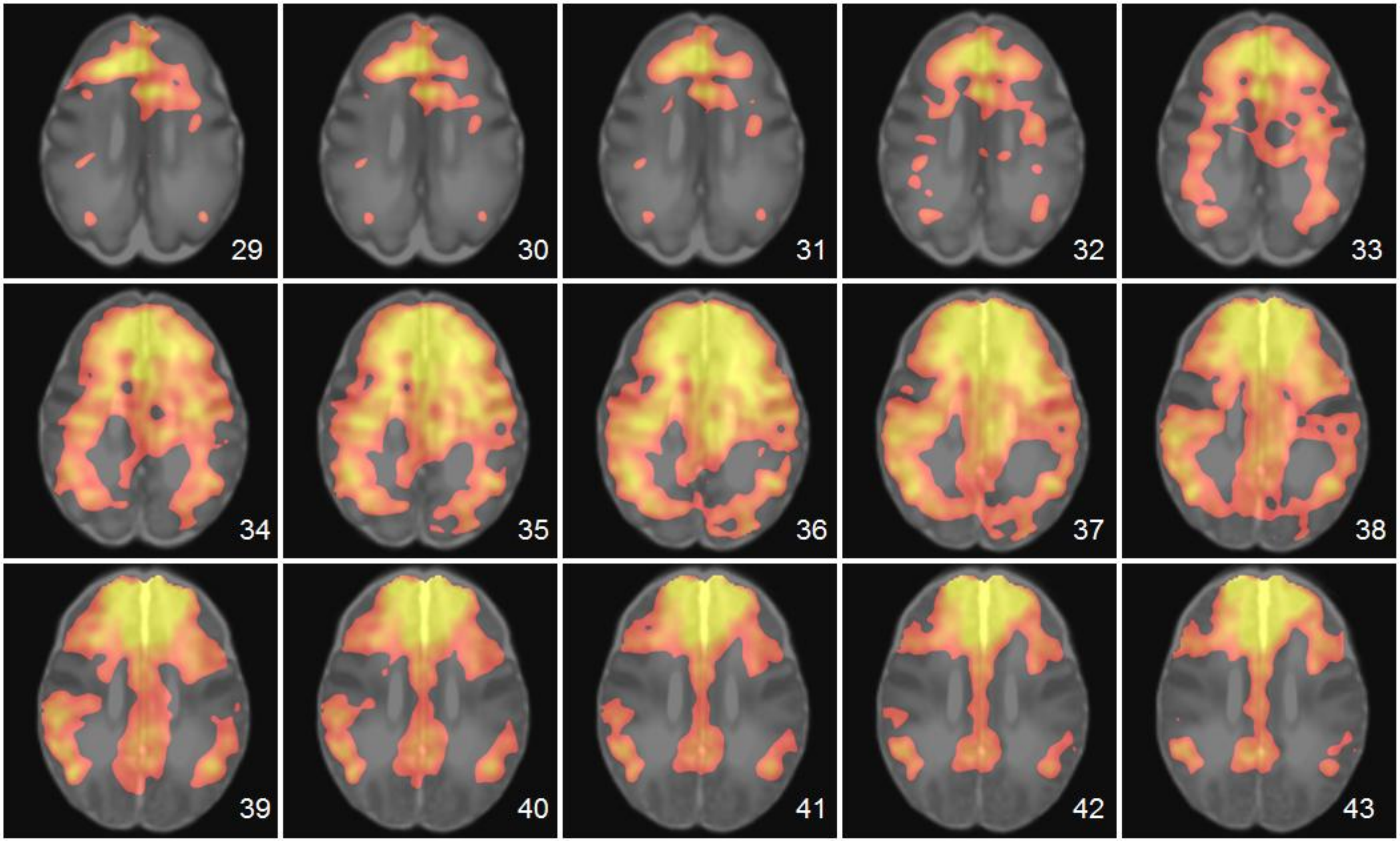
to the corresponding template frame

to the reference space

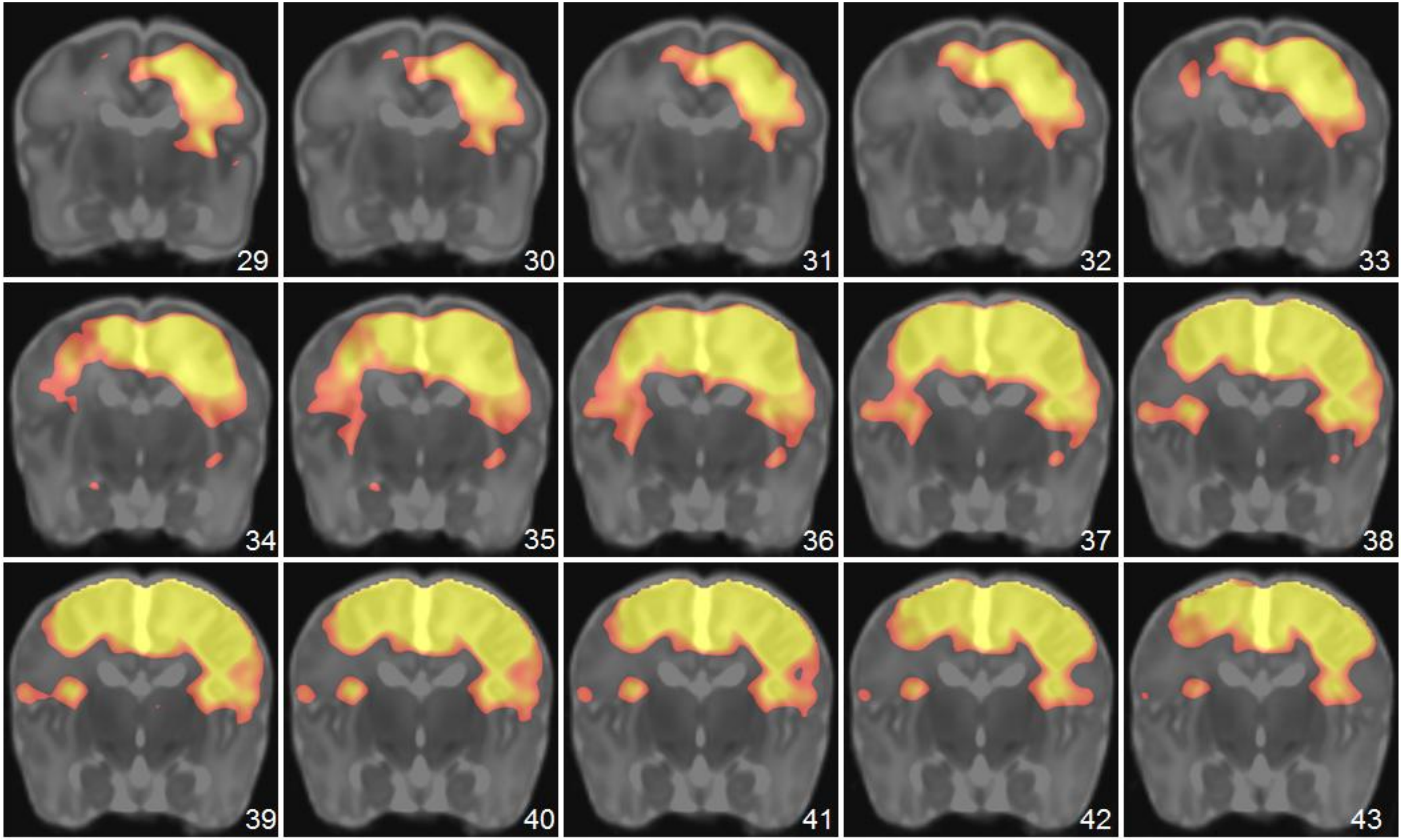
to the template frame at time-point *t*

$$\bar{C}(t) = \frac{\sum_{k=1}^{m} w(t_k, t) C_k \circ \mathcal{T}_{\bar{I}(t_k) \to F_k} \circ \bar{\mathcal{T}}(t_k) \circ \bar{\mathcal{T}}(t)^{-1}}{\sum_{i=k}^{m} w(t_k, t)}$$

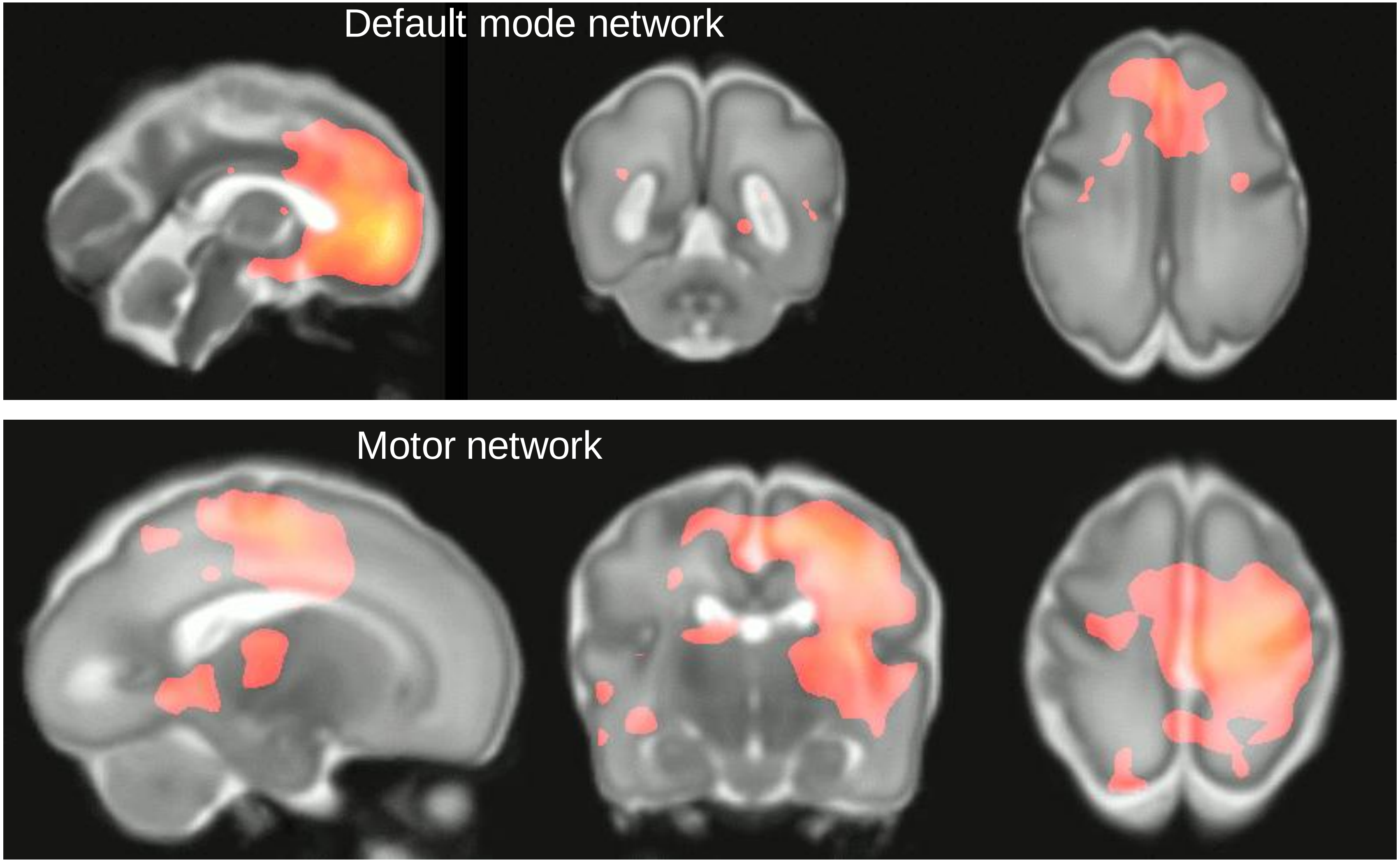
Model of developing default network



Model of developing motor network



Models of developing brain networks



Conclusion

- The presented model revealed the development of brain networks during 3^{rd} trimester of pregnancy
- The results have shown for the first time the presence of default mode network before birth
- The detailed paper by Valentina Doria et al. describing this important medical finding and more statistical analysis is under review
- Future work: Including more data in the model and validation

Thank you for your attention

4D probabilistic atlas

- Similar methodology with affine registration is being used to build 4D brain tissue probability maps (still under construction)