Characterizing gradients in cortical connectivity: Assessment and applications of manifold learning

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Introduction

Anatomical description of the human connectome has largely focused on delineating distinct cortical areas and network modules using various forms of categorical clustering. However, such approaches are limited in revealing the presence of: 1. broader gradations across distinct parcels; and, 2. gradual transitions between distinct areas, as previously demonstrated in cytoarchitectonic data. Evidence from gold-standard tract- tracing studies in the macaque monkey indicates the presence of stepwise gradations in patterns of connectivity. For example, direct projections occur predominantly between areas that are one level away in the architectonic hierarchy. In the frontal lobe, this pattern of progressive architectonic differentiation is spatially organized along orthogonal gradients spanning the dorso-ventral and rostro-caudal axes. Nonetheless, current applications of clustering methods to connectivity data acquired with MRI are not optimized to capture these overarching patterns. Previous studies have used MRI-based in vivo methods to investigate the similarity in the connectivity profiles of thousands of voxels simultaneously, and has shown the ability to identify boundaries between regions featuring a sharp transitions. However the presence of gradients of connectivity across regions has been thus far been neglected. Here we employed an original manifold learning method to recover complex connectivity structure, such as the overlapping gradients documented by the neuroanatomical literature.

Methods

We have used the 'dense connectome' derived from Human Connectome Project (HCP) [3,4] as the input to manifold learning algorithm, consisting of total 91282 cortical and subcortical nodes. The connectome was non-linearly decomposed into a set of spatial maps, which we call connectivity gradients (Fig 1a) [2]. The gradients represent sets of well-known resting state networks and relationships between them. Here we hypothesized that the set of gradients derived from resting state can be used as a basis set for the macroscale connectivity patterns [1].

To test this hypothesis, we have tested if the gradients can approximate the activation patterns observed in 7 tasks used in HCP. For each task, we have re-expressed each volume in time-series as a linear combination of 300 gradients derived from resting state (Fig 1b). For each subject and state, the weights of respective gradients were averaged.

We have trained a SVM with L1-penalty to classify between states within each task - fixation, control task and main task. L1 penalty allowed to get a sparse solution. The goal was to get reasonable classification accuracy with the most sparse set of gradients possible. We report accuracies for training, test and validation sets, each consisting of approximately 90 subjects

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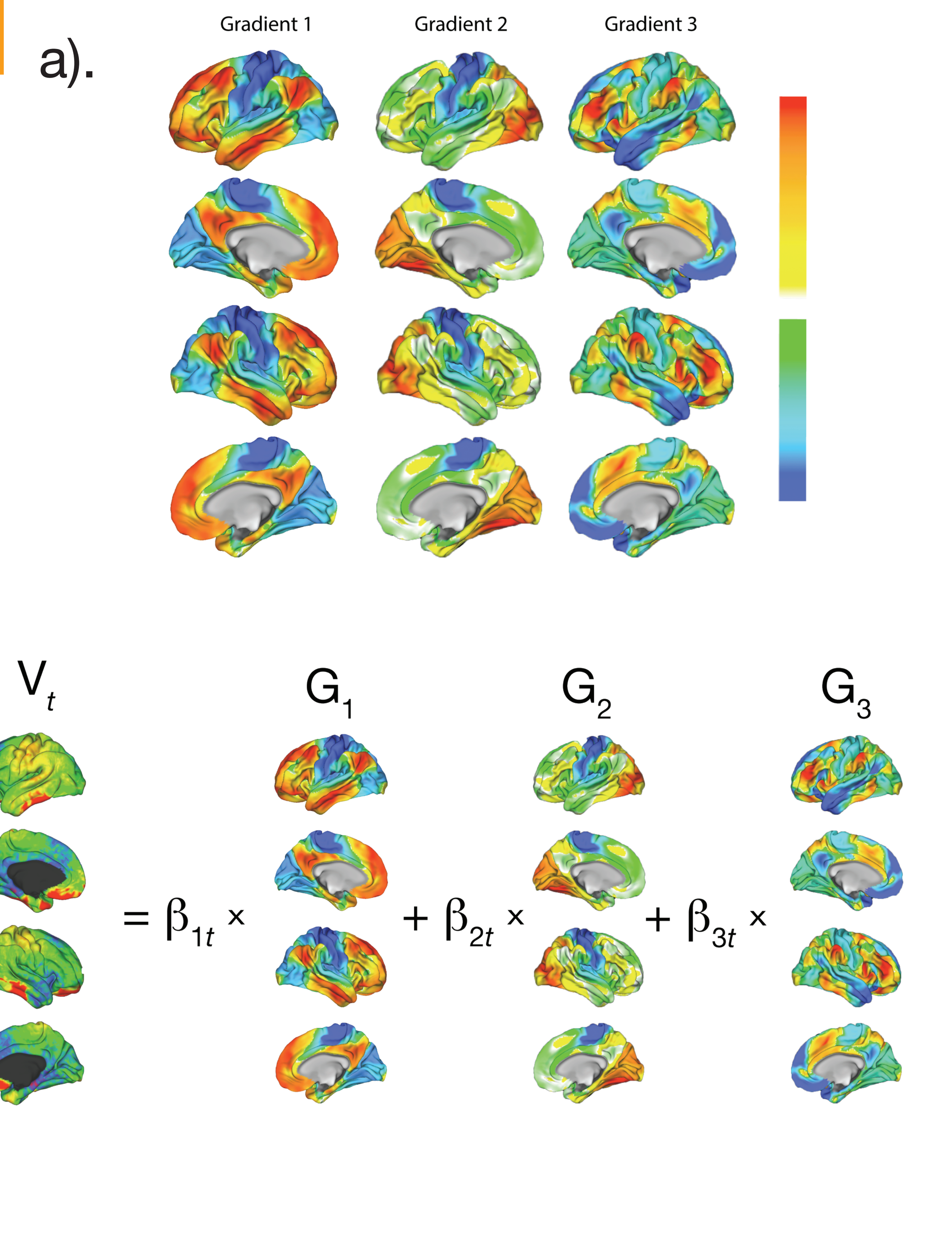

Results

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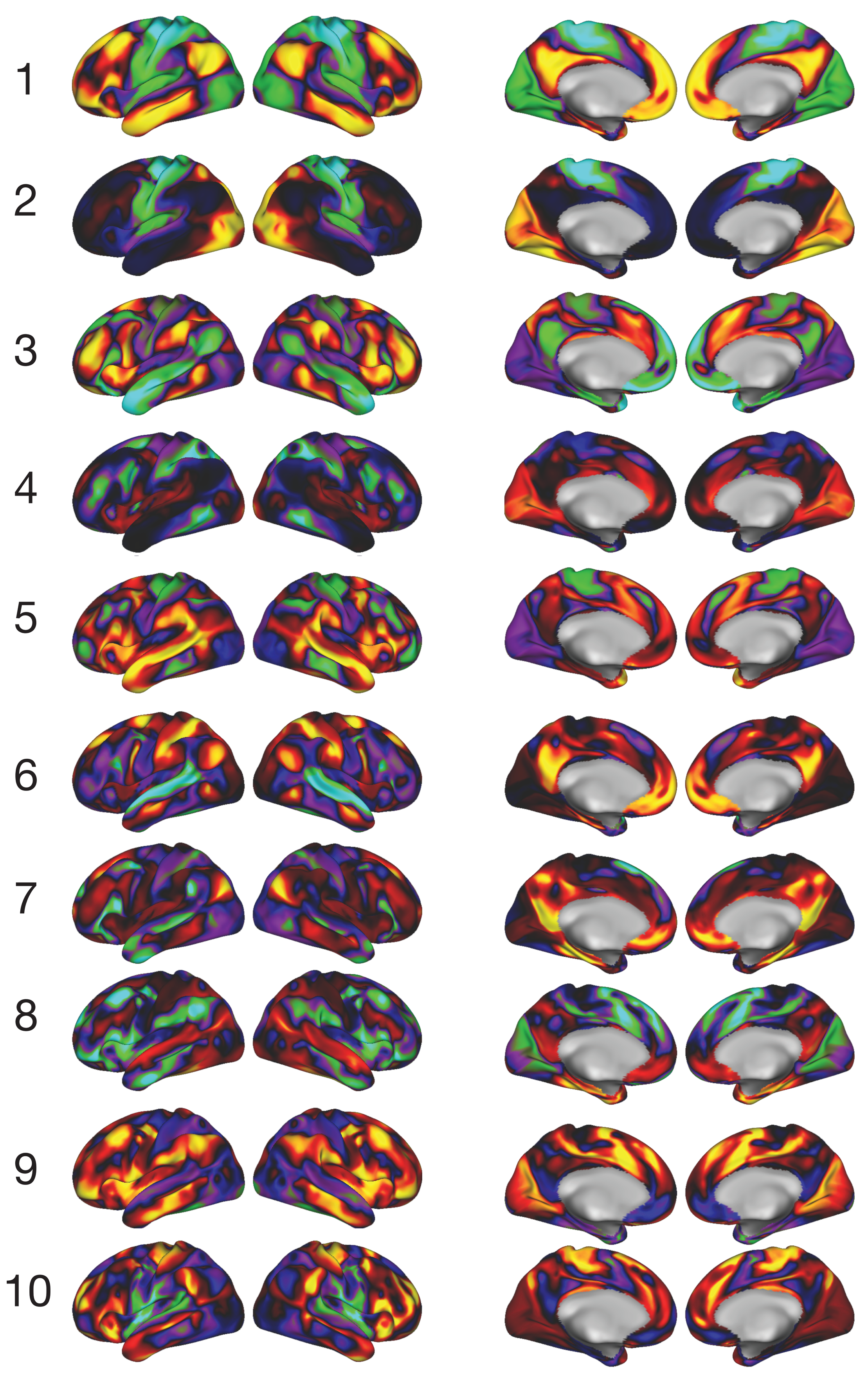

Fig. 2. Ten gradients based on resting state connectivity.

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Fig. 2 Average gradients timecourses (N=50) in WM task. Blue line represents run 1, orange - run 2. Red background represent 2-back condition, green - 0-back, white - fixation, brown - 2-back and 0-back switched between runs.

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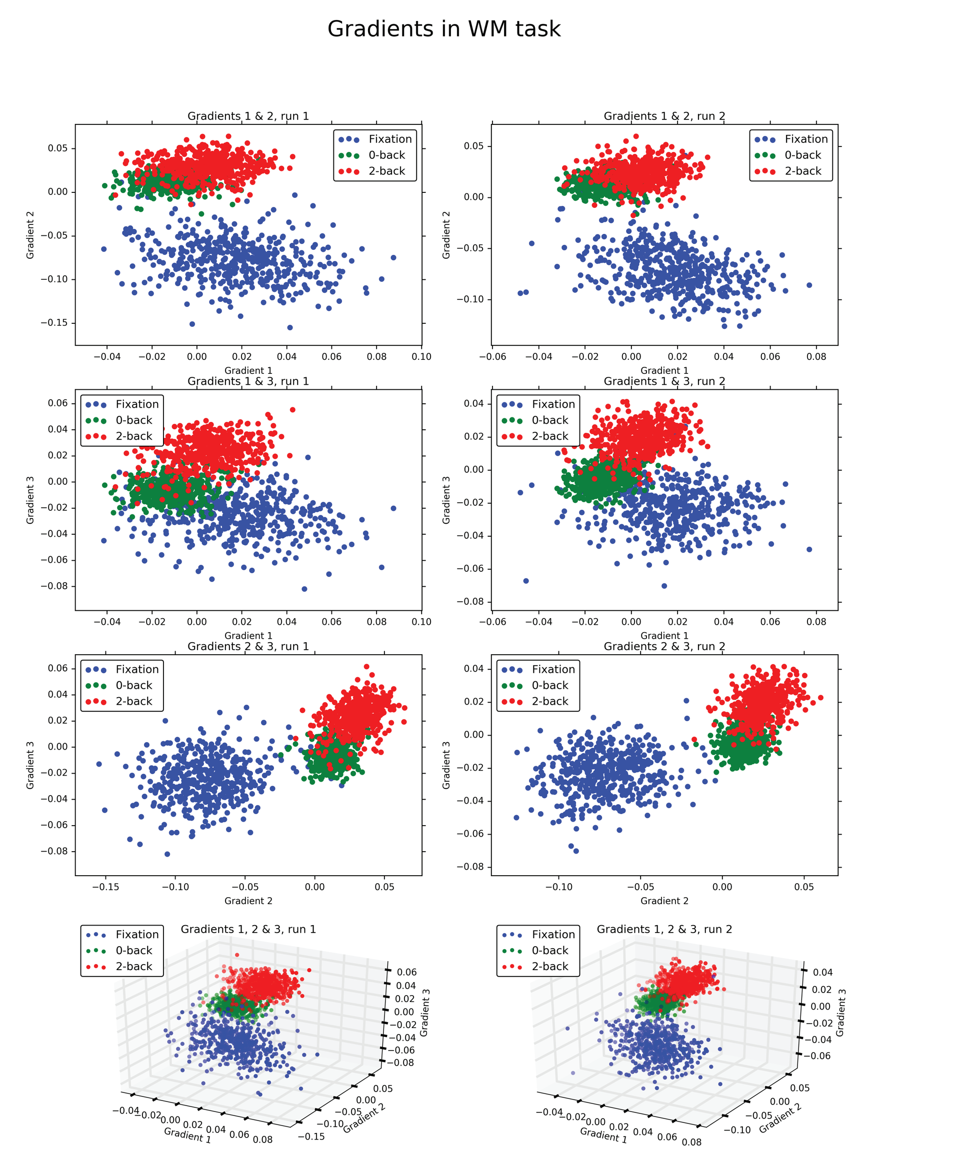

Fig. 3. States within WM task in space defined by 3 gradients. The plots indicate that conditions within n-back task are clearly separated in this space.

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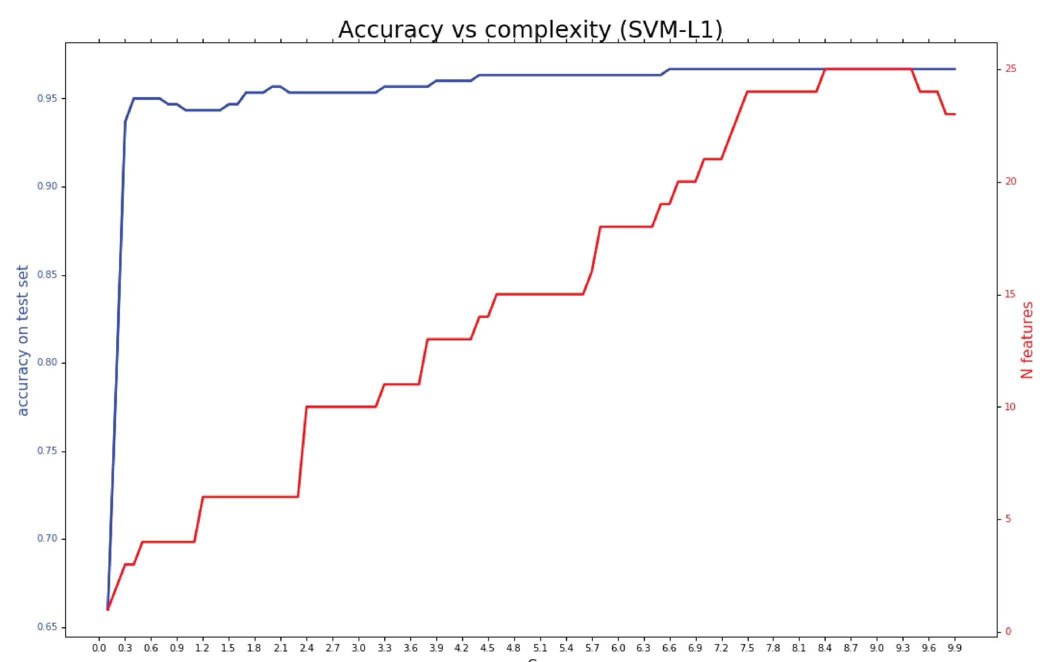

Fig. 4. Model selection procedure. 3 gradients are sufficient to achieve very high classification accuracy within the n-back task.

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Task	TR	TE1	TE2	TE3	Gradients	C	Comments
WM	94.4	94.4	97.8	94.4	1, 2, 3	0.5	
Social	92.1	92.5	92.4	91.7	1, 2, 4, 5	0.3	
Emotion	91	91	91.9	91.9	1, 2, 3, 6, 19, 23	0.5	
Relational	71.3	64	72.8	64.8	1, 2	0.5	Match/Relation confused
Motor	99.4	67.2	96.7	66.7	1	0.5	Poor run2 prediction
Gambling	77.3	58.5	78.6	60	2, 3	0.5	Loss/Win confused
Language	69.7	59.4	70.1	61.3	3	0.3	Fix/Maths confused

Fig. 5. Classification accuracies and selected gradients for all 7 HCP tasks. TR - training set, TE1 - test set 1, TE2, TE3 - independent test sets (different subjects)

Conclusions

1. Gradients derived from RS represent well-known networks and relationships between them (Fig 2)

2. Gradients show remarkable consistency across subjects and sessions (Fig. 3)

3. Relatively good classification accuracy could be achieved by manually drawing lines on a 2D plane (Fig. 4)

4. Very small subsets of gradients allow to achieve high classification accuracies of states within tasks (Fig. 5 and 6)

5. Low-frequency gradients perform best for tasks which engage consistent sets of large-scale networks (Fig. 6)

6. Further research is needed for development and interpretation of individual connectivity gradients

References

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