THE ROLE OF DORSAL ANTERIOR CINGULATE CORTEX IN MOTOR CONTROL

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“God uses his people in ways one can not imagine.”
Outline

1) Purpose of the Study
2) Anatomy and Function
3) Highlights from Other Literature
4) Research Question
5) Methods and Materials
6) Results
7) Conclusions
8) Suggestions for Future Research
Purpose of the Study
My study addresses the role of dorsal anterior cingulate cortex in motor control.
Anatomy and Function
Cingulate Cortex

• The cingulate cortex resembles a “collar” surrounding the corpus callosum.

• Anterior cingulate cortex is situated in the medial frontal cortex.
Dorsal Anterior Cingulate Cortex

Anterior cingulate (ACC)
(d; dorsal, v; ventral, perigenual)

- Dorsal ACC: Brodman areas 24 and 32. Has a role in Cognitive function.
Functional Heterogeneity in dACC:

- Motor control
- Working memory
- Depression
- Reward processing
- Decision-making
- Error detection and conflict monitoring
To study the role of dACC in motor function we looked at its relation with two other parts of motor cortex:

• Primary Motor Cortex (BA4).
  a) Contralateral to right index finger region of M1.

• Medial premotor cortex also called 6b or Supplementary Motor Area (SMA).
  a) SMA is hierarchically higher than M1.
Highlights from Other Literature
SMA in Humans is Analogous to Monkey 6aa and 6ab

In the macaque monkey, a caudal (posterior) area 6aa and a rostral (anterior) area 6ab on the medial surface of the brain correspond reasonably well to the human SMA, respectively (Matelli et al., 1991, Tanji et al., 1994).

Perpendicular line crossing the anterior commissure (Vca)
The intersection of the bicommissural line (CA-CP)
Location of motor areas in the medial wall of the hemispheres of the monkey

- Picard, N., & Strick (1996) have tentatively associated the dACC of humans with the CMAr of monkeys.

- There is substantial evidence that dACC is anatomically connected to the motor system:

  - Evidence from anatomical pathway tracing suggests that the dACC projects directly to the SMA in monkeys (Luppino et al. 1990; Matelli et al. 1991; Morecraft & Van Hoesen 1992).
Functional Evidence for Involvement of dACC in Motor Control

I. There is clinical evidence that dACC is functionally involved in motor control (Devinsky et al., 1995; Mesulam, 1981; Fellows, 2005; Milham & Banich, 2005).

II. Electrical stimulation in animals has also been used to demonstrate a motor role for dACC (Luppino et al., 1991; Picard & Strick, 2001).

III. Neuroimaging studies have confirmed that motor regions of the human dACC are activated during manual movement (Paus et al., 1993, 1998).
Functional Connectivity of dACC in Motor Control

The role of the dACC in motor control is under-characterized.

The quantitative analysis of connectivity requires sophisticated mathematical and statistical techniques.

Previous studies using resting-state undirected functional connectivity analysis have shown:

• The anterior midcingulate cortex is involved in motor control (Hoffstaedter et al., 2013).

• The dACC is involved in selecting and preparing the appropriate behavioral responses to achieve higher-level goals (Shulz et al., 2011).
What Is Missing from the Field?

- A wide gap currently exists between our understanding of neurocognitive network structure, function, and dynamics and a deeper understanding of human behavior.

- To better understand human behavior, a network approach to brain function is needed.

- We computed both directed and undirected functional connectivity between the dACC and SMA to investigate the role of the dACC in motor control.
What is a Brain Network?

• A brain network is a biological realization of a mathematical entity called a graph.

• A network consists of nodes connected by edges.

• In our study, an individual voxel standing for a brain region represents a node.

• These projects seek to identify and quantify functional network edges through the use of functional connectivity analysis.
What is Functional Connectivity (FC)?

• Statistical dependencies (correlation or regression between nodal activities) are derived from time series.

• The time series come from the variety of types of neural data including EEG, MEG, ECoG and blood oxygenation level–dependent (BOLD) functional MRI (fMRI).

• Able to measure the spatial path that information follows from one region to another region.
Research Question

What is the role of dACC in motor control?

- What is the functional relation of the dACC with/to the SMA and M1 using both undirected and directed functional connectivity?
Measuring functional connectivity: We used established methods for characterizing inter-regional interactions:

- Directed FC
- Undirected FC
- AutoRegression coefficient
- Pearson product-moment correlation coefficient (PMCC)

Asemi et al., 2015
Functional Connectivity

• The strength of undirected functional connectivity of one ROI with another was estimated by the magnitude of the PMCC computed using the cor function in the R software environment.

• The strength of directed functional connectivity from one ROI to another was estimated by the magnitude of a t-statistic from significance testing of the corresponding AR model coefficient computed in the GLM function in the R software environment.

a) This strength thus served as a metric for the dynamic causal relationship between the time series, and is similar to Granger causality in being derived from the MVAR model.
Methods and Materials
BOLD + well-validated image processing + Statistical analysis techniques

Specific demands of the behavioral paradigm

Functional connectivity between dACC and SMA
Subjects in two Projects

• The subjects for both projects come from the same group of adolescents.

• In project one: 11 Healthy adolescent participants
• In project two: 10 Healthy adolescent participants
Age of participants in both tasks: Coordinated motor task and nb-task

![Graph showing the number of subjects for different ages.](image-url)
4) Methods and Materials

Project 1
Behavioral Paradigms

Projects

1. Coordinated unimanual finger-movement in response to exogenous visual stimuli.
   Tapping-Coordination (TP task)
   vs Rest
   Control

2. Coordinated unimanual finger-movement in response to exogenous visual stimuli.
   Tapping-Coordination (TP task)
   vs n-back working memory
   Control
Project 1

Task: 3 conditions

Measures: UFC & DFC

Subjects

Two Pairs

Periodic
Pseudo-random
Rest

Task vs Rest
Periodic vs Pseudo-random
Age

SMA and dACC
M1 and dACC
Results

a. Activation
b. UFC
c. DFC
d. AGE
Activation Map
Task-related BOLD activation maps. Activation patterns are shown for the conjunction of the two task variants (*periodic and pseudo-random*) averaged across participants. Significant activation clusters (*p* < 0.01, cluster level) are overlaid on a mosaic of axial views.
Undirected Functional Connectivity (UFC)

I. Task vs Rest

II. Periodic vs Pseudo-random
Undirected Functional Connectivity (UFC) Results

- Comparisons of **task vs. rest** conditions on the undirected functional connectivity (PMCC) between the **dACC** and the **SMA** were not significant by either the parametric paired t-test or the nonparametric Mann-Whitney-Wilcoxon signed-rank test.

- The same was true between the **dACC** and **M1**.
Undirected Functional connectivity (UFC):
By contrast, comparison of Periodic and Pseudo-random task conditions revealed that the correlations both between dACC and SMA, and between dACC and M1, were significantly greater in the Periodic than the Pseudo-random condition.
Directed Functional Connectivity

I. Task vs Rest
II. Periodic vs Psudo-random
Directed Functional Connectivity (DFC):
The influence from dACC to SMA was significantly greater for task than rest, but the influence from SMA to dACC did not significantly differ (**p < 0.01).
Directed Functional connectivity:
Note that the distribution for the influence from dACC to SMA during the task is both more compact than rest and elevated above the distribution during rest.
Directed Functional Connectivity:
The group mean and standard error of influence in both directions between the 2 ROIs (dACC to M1, M1 to dACC) for task (blue) and rest (red) conditions.
Directed Functional Connectivity:
The influence from dACC to SMA was significantly greater for periodic than pseudo-random conditions, but the influence from SMA to dACC did not significantly differ.(**p < 0.01).
Age:

The task-specific modulatory influence from the dACC to the SMA was independent of age in all conditions.
Methods and Materials → Project 2
Behavioral Paradigms

Projects

1. Coordinated unimanual finger-movement in response to exogenous visual stimuli.
   Tapping-Coordination (TP task)
   vs
   Rest
   Control

2. Coordinated unimanual finger-movement in response to exogenous visual stimuli.
   Tapping-Coordination (TP task)
   vs
   n-back working memory
   Control
Projects 2

Task: 2 conditions

- 2back
- 0back
- Tapping-Coordination

Measures: UFC & DFC

- 2Tasks (Tapping vs nback)
- Age

Subjects

Two Pairs

- SMA and dACC
- M1 and dACC
Results

a) Undirected Functional Connectivity
b) Directed functional connectivity
c) Age
Undirected Functional Connectivity (UFC) :

![Graph showing PMCC values for different conditions and regions](image-url)
DFC Results
Directed Functional Connectivity (DFC):
The group mean and standard error of influence in both directions between the 2 ROIs (SMA to dACC, dACC to SMA) for nb-task (blue) and tp-task (red) conditions.
The group mean and standard error of influence in both directions between the 2 ROIs (dACC to M1, M1 to dACC) for nb-task (blue) and tp-task (red) conditions.
Age results

The task-specific modulatory influence from the dACC to the SMA was independent of age in all conditions.
Conclusions

- Conclusion 1
- Conclusion 2
- Conclusion 3
The dACC is not just involved in motor movement, but has a modulatory role on another motor control region.

- That the directional influence from the dACC to the SMA significantly distinguished task from rest suggests that the dACC may reside at a hierarchically higher organizational level than the SMA in motor control.

- The unimanual visumotor task, in which the dACC selectively modulates the SMA during visually coordinated unimanual behavior in adolescents, showed significantly greater influence from dACC to SMA than in the working memory task, thus suggesting a role for dACC in motor control that is different in the two tasks.

- According to our results, each task (nb-task or tp-task) employed different networks based on the nature of the motor response.
Predictable vs Unpredictable Stimulus in the Coordinated Movement Task

• The dACC activity was more tightly coupled with SMA and M1 when the stimulus was more predictable (Periodic) as compared to when it was less predictable (Pseudo-random).

• The results showed that there is a significant difference between Periodic and Pseudo-random conditions in directed functional connectivity from the dACC to the SMA.
The Maturing of dACC Related to Motor Control

In both studies, we sought to understand if the dACC of healthy adolescents is uniquely involved in motor control.

• Yes, dACC is involved in motor control at the adolescent stage of healthy brain development.

• Motor control, especially in motor coordination is established by the time of adolescence.

• From our study, the role of the dACC as an important brain area for the mediation of task-related motor control is in place during adolescence and may continue into adulthood (Asemi et al., 2015).
Limitation and future research
We identified 3 limitations in our studies.
Our study used adolescent subjects not adults.
Small Sample Size

The number of subjects in this study was small and this limited the number of interactions that could be studied.
Our statistical analysis of time series did not allow us to determine the anatomical pathway over which modulatory signals might be conveyed between areas.
Future Directions

These findings should be of general interest to those studying motor control and neuropsychiatric illnesses in adolescents and adults:

Further testing needs to be done:

i. The role of dACC in motor control in adults.

ii. Coordination (synchronization) vs Continuation in dACC to SMA interaction in adults and adolescents.

iii. Synchronization vs Syncopation in dACC interaction with SMA in adults and adolescents.

iv. Repeat these experiments in adolescent attention deficit hyperactivity disorder (ADHD), adolescent schizophrenia and adolescent Obsessive-Compulsive Disorder (OCD).
The end!
Thank you for your attention!
Any questions?
GC

A. Restricted Model

\[ x_t = \sum_{i=1}^{m} \alpha_{1i} x_{t-i} + \varepsilon_{1t} \]

\[ \text{Var} (\varepsilon_{1t}) = \sum_{1} \]

\[ F_{X \to Y} = \ln \frac{\sum_{1}}{\sum_{2}} \]

B. Unrestricted Model

\[ x_t = \sum_{i=1}^{m} \alpha_{2i} x_{t-i} + \sum_{i=1}^{m} \beta_{2i} y_{t-i} + \varepsilon_{2t} \]

\[ \text{Var} (\varepsilon_{2t}) = \sum_{2} \]

\[ \beta_{2i} \neq 0 \]

Then Y & X Granger causes X
Project 1
Task: 3 conditions
Analysis: UFC & DFC

Project 2
Task: 3 conditions
Analysis: UFC & DFC
\[ t_{\hat{\beta}} = \frac{\hat{\beta} - \beta_0}{\text{s.e.}(\hat{\beta})}, \]
Functional magnetic resonance imaging (fMRI): Functional neuroimaging

- To detect correlations between brain activation and a task the subject performs during the scan.

- Based on Blood-Oxygen-Level-Dependent (BOLD): Hemodynamic response (HDR)

- A subject performs a cognitive task -> neurons become active -> deoxyhemoglobin ↑ -> local blood flow -> oxy-hemoglobin ↑ -> increase in the fMRI signal