The Capacity to Engage Difficult-to-Reach, Energetically Costly Brain States Predicts Learning in Complex Cognitive Tasks

Alexanndra Angebrandt, Ramsey R. Wilcox, Aron K. Barbey

University of Nebraska-Lincoln, Center for Brain, Biology, and Behavior

Structural Biomarker of State Dynamics

- Learning involves building upon prior experience to meet the demands of an unfamiliar task.
- Within the brain, this process may involve the **ability to dynamically engage connections** that have not been strongly established by prior experience.
- Engaging these weakly established connections requires **substantial metabolic energy**, making the associated **brain states harder to access and sustain**[1].
- The brain's **structural connectivity constrains functional dynamics**[2] by restricting the set of accessible states and determining the amount of energy required to engage each state.
- **Modal controllability**, as defined by Network Control Theory, quantifies how effectively individual brain regions facilitate **high-energy transitions to difficult-to-reach states.**

Is learning constrained by the brain's structural capacity to support difficult, energetically-demanding state transitions, as captured by modal controllability?

Experimental Protocol

Large, multi-domain intervention trial[3]

- **16-week intervention** including cognitive, physical fitness, and mindfulness training
- **Current study** uses subset of participants that completed cognitive training and MRI

Intervention	n	Age mean (sd)	Sex (%M)	Timeline & Session Type			
EF + Fitness	43	23.3 (4.8)	44%	12 Fit	8 Fit 4 EF	8 Fit 16 EF	
EF + Fitness + Mindfulness	41	23.6 (5.2)	35%	10 Mind 2 Fit	12 Fit	10 Fit 2 EF	4 Fit 8 EF
Visual Attention	43	24.7 (6.9)	61%	48 Visual Attention			
Total Sample	127	23.9 (5.7)	47%				

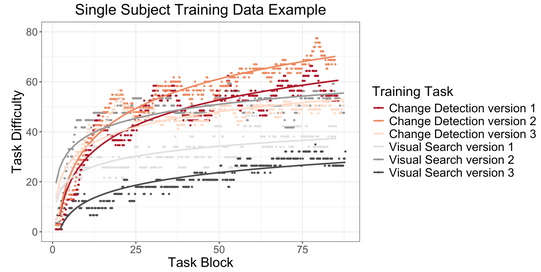
EF: Executive function, Fit: Fitness, Mind: Mindfulness

- Effect of other training modalities evaluated with Fat-Free VO_2-max and Mindful Attention Awareness Scale (MAAS)[4]
- Baseline EF ability measured by Figure Series[5]
- Modal controllability calculated from normalized structural connectomes (DTI) using *nctpy*[6] in python

Executive Function Training

Cognitive Task	Scientific Basis
Working memory (Dual N-back)	Jaeggi et al., 2008; 2010
Working memory (Visuospatial)	Thorell et al., 2008
Working memory (Updating)	Dahlin et al., 2008
Cognitive control (Dual task switching)	Karbach & Kray, 2009
Reasoning (Visuospatial)	Mackey et al., 2010
Planning (Tower of London)	Shallice, 1982
Reasoning (Analogical)	Wechsler, 2008
Change detection	Gaspar, 2013
Visual search	Harrison, 2013

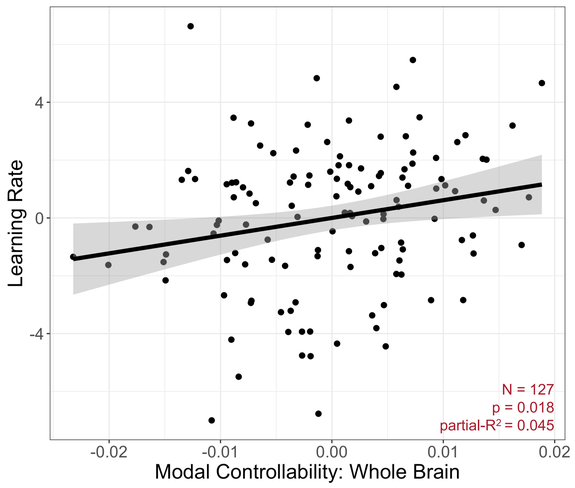
All tasks have **adaptive difficulty:** performance determines difficulty of the next training block. Reaching higher difficulty levels over time reflects task learning.



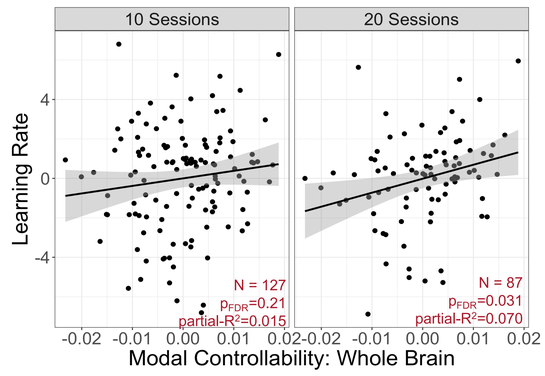
Learning rates were estimated separately for each subject with log-linear mixed-effect models with random effect of training task.

Access to Difficult-to-Reach States Predicts Learning

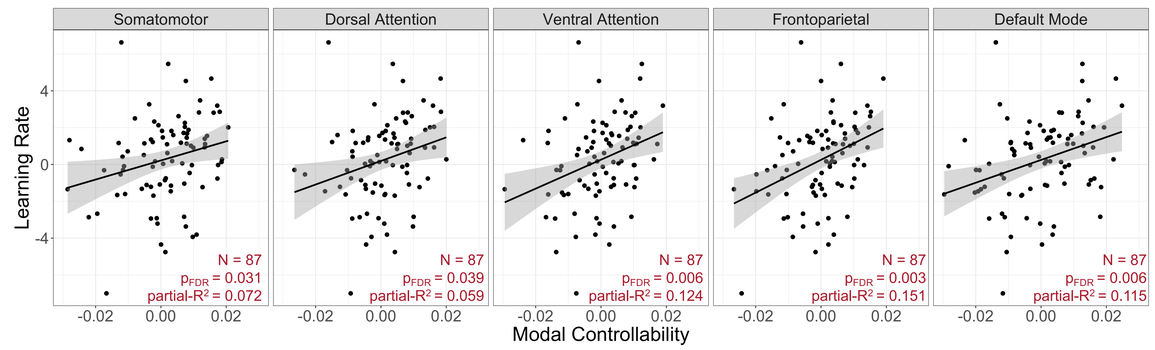
All regression models include covariates for age, sex, △ Fat-Free VO_2-max, △ MAAS, baseline Figure Series, and # cognitive training sessions.



The **capacity to engage difficult-to-reach states promoted learning** in skill-based executive function training *(left)*. Recruitment of weak connections was especially **critical at the higher difficulty** levels reached in later training sessions *(below)*.



Modal Controllability in Task-Relevant Networks Explains Individual Differences in Learning



Structural brain networks that support network transitions to difficult-to-reach states, as reflected by high modal controllability, promote faster learning during executive function training.

Discussion & Future Directions

- The **adaptive difficulty** of the training program established a complex, dynamic environment that required participants to build upon their prior experience to solve novel problems.
- Successful task completion and progression to the next training stage (i.e., learning) increasingly relied on **modal controllability** at later stages of training when the complexity of tasks required modification of problem-solving strategies.
- The enhanced **dynamic flexibility** afforded by structural networks with **high modal controllability predicted overall learning** across a variety of executive function tasks.
- Additional research is needed to specify the role of individual brain regions in facilitating transitions to difficult-to-reach states and their impact on distinct facets of executive function.

Acknowledgements

We deeply appreciate the INSIGHT team who made this project possible.

This research was supported by funds from the Office of the Director of National Intelligence (ODNI), Intelligence Advanced Research Projects Activity (IARPA), via Contract 2014-13121700004 to the University of Illinois at Urbana-Champaign (PI: Barbey), National Science Foundation Graduate Research Fellowship Program under Grant No. DGE 21-46756 (author A.A.), and was conducted in part at the Beckman Institute for Advanced Science and Technology of the University of Illinois at Urbana-Champaign (UIUC-BI). Any opinions, findings, and conclusions or recommendations expressed in this material are those of the author(s) and do not necessarily reflect the views of the funding agencies.

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Contact Information

A. Angebrandt: aangebrandt2@unl.edu