“Sam Castillo

NBL 399 Thesis Outline

**Objective**

I’m aiming to explore a variety of fMRI experimental paradigms in hopes of gauging to what degree, if any, different paradigms lead to different neural responses when targeting the same network. I would like to gain a better understanding of how investigators’ methods affect the relevancy of the results. Specifically, I’d like to analyze paradigms designed to elicit activity in memory-encoding networks.

Main question: How do fMRI experimental paradigms influence the neural response when analyzing neural correlates of memory-encoding?

**Approach**

Analyze various fMRI experimental paradigms designed to explore neural networks involved in memory encoding. Compare consistency and clarity of results across paradigms to determine to what degree, if any, different paradigms elicit activity in different neural components.

**Outline**

1. fMRI: A brief overview
   1. What is fMRI?
   2. How fMRI differs from MRI; brief explanation of how MRI works
   3. Discuss the BOLD Signal
   4. What sort of data can an fMRI experiment obtain? How does it provide insight to neural networks, underlying processes, and psychological behavior?

*Overview of Functional Magnetic Resonance Imaging,* **Glover 2011**

1. Limits and possibilities of fMRI experimentation
   1. Physical limits within the scanner (motion, claustrophobia, metal)
   2. Experimental paradigms must be designed practically and according to the scanner’s abilities
      1. Interspace intervals, block-design vs event-related design, stimulus type and duration
   3. Statistical analysis of fMRI data is prone to false positives unless effects are strong
      1. Noise is abundant, both physically and statistically

*Overview of Functional Magnetic Resonance Imaging,* **Glover 2011**

*(1),* **James 2014**

*Comparison of fMRI paradigms assessing visuospatial processing: Robustness and reproducibility,* **Schuster 2017**

*(2),* **Amaro Jr. 2006**

1. An overview of memory
   1. Brief overview of different categories of memory
      1. Atkinson-Shiffrin: sensory, short-term, long-term
   2. Process of memory: encoding, consolidation, retrieval

Atkinson, R.C.; Shiffrin, R.M. (1968). "Chapter: Human memory: A proposed system and its control processes". In Spence, K.W.; Spence, J.T. (eds.). The psychology of learning and motivation. 2. New York: Academic Press. pp. 89–195.

1. Summary of our understanding of the neural correlates of memory-encoding based on fMRI studies
   1. Medial temporal lobe
   2. Anterior cingulate cortex
   3. Posterior parietal cortex
   4. Fusiform gyrus

*The Hippocampus Is Coupled with the Default Network during Memory Retrieval but Not during Memory Encoding*, **Huijbers 2011**

*Test-Retest Reliability of fMRI Brain Activity during Memory Encoding*, **Brandt 2013**

*Mechanisms Underlying Encoding of Short-Lived Versus Durable Episodic Memories,* **Sneve 2015**

*What Neural Correlates Underlie Successful Encoding and Retrieval? A Functional Magnetic Resonance Imaging Study Using a Divided Attention Paradigm*, (3)**Kensinger 2003**

1. Selected paradigms designed to analyze memory and memory-encoding
   1. N-back
   2. Sternberg
   3. Scene-encoding
   4. …more to come
2. Comparison of results/memory encoding networks generated through these paradigms
   1. Discussion of consistency/inconsistency across results from paradigms
3. Conclusion: do we know as much about neural networks as we think we do?
   1. Suggestion: we don’t.
4. fMRI: A brief overview
5. What is fMRI?
6. How fMRI differs from MRI; brief explanation of how MRI works
7. Discuss the BOLD Signal
8. Overview of paradigms (task-based & resting state)
9. Data analysis—stats, corrections, etc.
   * 1. GLM
     2. Multiple Comparison Correction
10. What sort of data can an fMRI experiment obtain? How does it provide insight to neural networks, underlying processes, and psychological behavior?
    * 1. This is a lead-in to the next section.
11. fMRI Data Interpretation: Forward Inference, Reverse Inference, and Operationalization
    1. Forward and Reverse inference: Overview
    2. Operationalization and Inference
    3. Tal Yarkoni & Neurosynth
    4. Is Inference Trustworthy?
    5. The Significance of Adequate Operationalization
12. Have We Come to False Conclusions? (discussion of practical implications)
    1. Probably so, especially given how much we’re still learning as a field.
    2. Clinical relevance of falling short in fMRI analysis
       1. Psych diagnosis, eval, etc.
    3. False interpretations 🡪 False replications
13. Conclusion
14. Overview of where we are as a field
15. Future Directions of fMRI experimentation
16. Introduction: A Brief Overview of Neuroscientific Methodology
    1. Brain is Complex | Early attempts to understand it
    2. Case Studies
       1. Phineas Gage
    3. Bridge into functional localization
       1. Tools used
17. Overview of MRI & fMRI
    1. Signal Source
       1. BOLD Response
       2. HRF
18. Functional Localization via fMRI: Validity at Stake
    1. Inference: The Fundamental Basis of Data Interpretation
       1. Overview of Inference
          1. Reverse Inference
          2. Forward Inference
    2. Operationalization: The Fundamental Basis of Inference
       1. Statistical Analysis: An Operationalization of Experimental Paradigm
          1. GLM
          2. Type I and Type II Errors
          3. Unmeasured Factors
       2. Experimental Paradigm: An Operationalization of Theoretical Perspective
          1. Task-Based Functional Localization
             1. N-back example
          2. Shortfalls of Operationalization in Paradigm Design
             1. Replicability is NOT Validation of Operationalization
             2. Sullivan – Water Maze
          3. Attempts to Fix by Tightening only worsen the issue
19. Moving Forward
    1. Operationalization and Inference: Bridging the Gap
       1. Paradigm Design: Natural Stimuli
          1. Benefits & Results of Natural Stimuli
          2. Statistical Analysis Using Natural Stimuli
       2. Implementing Natural Stimuli in Other Cognitive Contexts
          1. Obstacles, advantages
20. Conclusion
    1. This isn’t a dismissal of previous approaches—we needed those to get where we are today
    2. But, our operationalizations must keep up with the field