Elucidating the causality in “causal brain circuits”: Theory, methods and applications

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Symposium

Recent work in statistical causal inference and philosophy of causation has re-invigorated discussion of causal mechanisms both within theoretical neuroscience and in statistical fields outside of neuroimaging. However, these advances have not yet been widely adopted within the neuroimaging and the OHBM community. Speakers in this symposium will discuss how neuroimaging studies can benefit from defining what counts as a causal explanation and how to infer such causal mechanisms from data. To make this tangible, all the talks will discuss these advances in the context of empirically assessing causality within or between brain circuits. In particular, we define causes by hypothetically asking "what would happen to Y if we were to fix the value of X"

Each talk will discuss problems and solutions for questions of the following variety:
(i) “brain circuit X consists of strongly connected regions Y and Z”
(ii) “brain circuit X has Y function”
(iii) “brain circuit X predicts Y clinical phenotype” or “brain circuit is a biomarker for depression”

Neuroimaging studies that answer these questions increasingly use statistical learning techniques with emphasis on good out-of-sample and out-of-study generalization. However widely used techniques to find important features or perform high dimensional regression fall far short of providing guarantees that the relationships implied learning are causal. Moreover, recent theoretical papers in brain and behavioral sciences have pointed out several theoretical problems in the causal explanations provided by “brain circuit X causes Y behavior” statements when behavior or phenotype is poorly defined.

Achieving the objectives of this symposium will introduce new theory and methods for solving the above questions more rigorously. These frameworks are particularly relevant to the OHBM community since measurements of brain organization and neurophysiological activity are inherently piecemeal. Thus measurements in every modality and scale are bound to suffer from irreducible confounding and underdetermination. While improving the resolution of measurement technologies such as MRI can help, technological solutions alone will not solve all the obstacles to causal inference. Incorporating ideas from emerging fields will spur new solutions to strengthen empirical conclusions of causation in neuroimaging and its translational applications.

Diversity: The organizers/speakers represent both early career and senior researchers. The symposium is multi-disciplinary. The speakers who will address the issue of taking causation more seriously span backgrounds that include neuroimaging, computational neuroscience, statistics, computational psychiatry and philosophy of science/mind. The symposium features two speakers who self-identify as women in STEM. Additionally, some

speakers are established faculty in related fields but new to OHBM.

Objective

Each talk may address more than one of these objectives:
1. Participants will learn interventionist and counterfactual accounts of causation and relevant statistical causal inference techniques for employing them in neuroimaging.
2. Participants will learn why perturb & measure approaches alone do not guarantee inference of causal relationships between brain circuits and phenotype.
3. Participants will learn two frameworks to improve conceptual characterization of phenotypes:
(i) evolutionary approaches to defining function of brain circuits
(ii) philosophy of science on "carving psychopathological phenomena at its joints" and implications for brain circuits to create RDoC constructs.
4. Participants will learn to model biomarker taxonomy and how this applies to psychiatric neuroimaging.

Target Audience

Accessible to anyone in the OHBM community. Of particular interest to scientists who conduct multi-species brain mapping, are involved in psychiatric neuroimaging studies, investigate functional/effective connectivity, or are familiar with ongoing issues regarding causal explanations in human brain mapping.

Presentations

What does it mean for brain regions to causally influence one another and why don't functional/effective connectivity count as causal.

I will review the causal inference literature with a focus on causal inference in high-dimensional systems. I will introduce the omitted variable bias equations that are prominently used in the causal inference literature and show how they may inform our way of thinking about functional connectivity results. The talk will analyze the emerging literature in neuroimaging with a causal lens, and spell out ways of estimating the causal validity of current approaches. A focus will be on integrative approaches, the use of data across many layers of analysis to estimate bias and variance of relevant estimators of causal interactions.

Presenter

Konrad Kording, University of Pennsylvania Philadelphia, PA
United States

Carving up brain functions from an evolutionary perspective

Neuroimaging studies often attempt to infer the functional roles of different brain regions by decoding the representations putatively necessary for specific computational processes. For that approach to succeed the computational processes must be delineated in a way that reflects the real functional organization of the brain. However, most of the definitions used today are inherited from a long history of philosophical thought that was not constrained by biological data and is increasingly challenged by neurophysiological studies. Here, I'll describe an approach for defining computational processes based on evolutionary history. I'll present a brief chronological

story of some of the major steps in brain evolution along the lineage leading from early animals to humans, resulting in a theoretical framework of brain organization that differs in important ways from classic models of cognitive psychology. I will suggest that this framework can offer a better set of target processes for neuroimaging investigation.

Presenter

Paul Cisek, University of Montreal Montreal, Canada
Canada

What kind of kinds are optimal for causal discovery in clinical neuroscience?

A primary aim of clinical neuroscience is to illuminate the neural mechanisms that give rise to psychopathological phenomena. Yet, there is disagreement and uncertainty about what the phenomena are—what the targets of empirical inquiry and causal explanation ought to be. Psychiatric neuroimaging has recently moved away from DSM categories in favor of constructs designating domains of behavioral functioning for which candidate brain circuits may be more readily identified (i.e., RDoC constructs). Is there a single correct way of carving psychopathological phenomena? What desiderata must brain-circuit based psychopathological "kinds" satisfy? The aim of this talk is to use conceptual tools on offer in philosophy of science to address these questions with an eye towards promoting constructive discussion about the best way forward for neuroimaging approaches to psychopathology.

Presenter

Jacqueline Sullivan, Western University London, Ontario
Canada

When do we need etiological brain-circuit biomarkers?

Clinical neuroimaging studies frequently report the discovery of biomarkers, that is, neuroimaging-derived predictors of some phenotype. Biomarkers may be used for a variety of purposes from enriching clinical trials to predicting risk to choosing treatments. Given the range of clinical applications, one might ask "Are all biomarkers created equal, or do some need to be more causal than others?" This talk will introduce a formal taxonomy for biomarkers and provide causal models to conceptualize desirable characteristics. Using this framework, I will discuss when brain circuit biomarkers need to be etiologically related to the disorder or some clinical phenotype. Finally, I will discuss strengths and limitations of employing simultaneous brain stimulation & imaging to finding more causal brain-circuit biomarkers.

Presenter

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