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Review

Foundational perspectives on causality in large-scale brain networks

Michael Mannino [a], Steven L. Bressler [a,b,*]

[a] *Center for Complex Systems and Brain Sciences, Florida Atlantic University, 777 Glades Road, Boca Raton, FL 33431, United States*
[b] *Department of Psychology, Florida Atlantic University, 777 Glades Road, Boca Raton, FL 33431, United States*

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Abstract

A profusion of recent work in cognitive neuroscience has been concerned with the endeavor to uncover causal influences in large-scale brain networks. However, despite the fact that many papers give a nod to the important theoretical challenges posed by the concept of causality, this explosion of research has generally not been accompanied by a rigorous conceptual analysis of the nature of causality in the brain. This review provides both a *descriptive* and *prescriptive* account of the nature of causality as found within and between large-scale brain networks. In short, it seeks to clarify the concept of causality in large-scale brain networks both philosophically and scientifically. This is accomplished by briefly reviewing the rich philosophical history of work on causality, especially focusing on contributions by David Hume, Immanuel Kant, Bertrand Russell, and Christopher Hitchcock. We go on to discuss the impact that various interpretations of modern physics have had on our understanding of causality. Throughout all this, a central focus is the distinction between theories of deterministic causality (DC), whereby causes uniquely determine their effects, and probabilistic causality (PC), whereby causes change the probability of occurrence of their effects. We argue that, given the topological complexity of its large-scale connectivity, the brain should be considered as a complex system and its causal influences treated as probabilistic in nature. We conclude that PC is well suited for explaining causality in the brain for three reasons: (1) brain causality is often mutual; (2) connectional convergence dictates that only rarely is the activity of one neuronal population uniquely determined by another one; and (3) the causal influences exerted between neuronal populations may not have observable effects. A number of different techniques are currently available to characterize causal influence in the brain. Typically, these techniques quantify the statistical likelihood that a change in the activity of one neuronal population affects the activity in another. We argue that these measures access the inherently probabilistic nature of causal influences in the brain, and are thus better suited for large-scale brain network analysis than are DC-based measures. Our work is consistent with recent advances in the philosophical study of probabilistic causality, which originated from inherent conceptual problems with deterministic regularity theories. It also resonates with concepts of stochasticity that were involved in establishing modern physics. In summary, we argue that probabilistic causality is a conceptually appropriate foundation for describing neural causality in the brain.

Keywords: Brain; Large-scale neurocognitive networks; Causality; Probability; Determinism; Brain connectivity

* Corresponding author at: Center for Complex Systems and Brain Sciences, Florida Atlantic University, 777 Glades Road, Boca Raton, FL 33431, United States.
E-mail address: bressler@fau.edu (S.L. Bressler).

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"The law of causality, I believe, like much that passes muster among philosophers, is a relic of a bygone age, surviving, like the monarchy, only because it is erroneously supposed to do no harm."

[Bertrand Russell (1913)]

1. Introduction

By virtue of what is one thing or event the cause of another thing or event? The question is an old and familiar one, and has been camouflaged in various cloths throughout the history of science, mathematics and philosophy. It is closely related to various other problems concerning the foundations of causality: what is the fundamental nature of causal relations? Is causality real, and *a fortiori*, ontologically independent of the mind, or is it merely an epistemic limitation? In the context of statistical analysis, are causal relations inherently deterministic or probabilistic? Finally, and perhaps most importantly for what follows: is causality affected by complexity? That is, is it necessary to expand our conception of causality to cover causal influences in the human brain, which may be affected by its properties as a complex adaptive biological system? Or, more germane to the current discussion, must the causal influences between neuronal populations[1] in complex brain systems be described in a more comprehensive way – with a different foundational conception – than influences in simple physical systems?

Historical as well as modern attempts to formulate an unambiguous conceptual description of causality are rich and plentiful; modern philosophers such as David Hume, Immanuel Kant, Bertrand Russell, Nancy Cartwright, Patrick Suppes, and Christopher Hitchcock, among others, have developed both ontological and epistemological accounts of causality. Moreover, modern mathematicians, statisticians, and economists, such as Austin Bradford Hill, Norbert Weiner and Clive Granger have developed methodologies for measuring causality with statistical tools from the perspective of stochastic processes. Nevertheless, the basic nature of causality within modern conceptions remains to be clarified, especially for complex systems such as the human brain. In this review, we address classical and contemporary work in philosophy, cognitive neuroscience, and statistics, and propose future research avenues of approach to a central, but unanswered question: what is the nature of causal influences in the human brain, specifically in large-scale brain networks? And more generally, what is the nature of causal influences in complex systems? It is highly doubtful that Hume or Kant considered what sorts of causality occur in organized complex systems, for example, coupled neuronal populations in the human brain; nevertheless, it is time, once again in the history of science, for the notion of causality to be *conceptually expanded*, this time into the study of brain networks. Given this ambitious claim, the central goal of this review is to examine, in the context of a complex biological system, whether the classical notion of causality is valid.

The classical concept of causality is discussed in more detail below. Here we note that even before the advent of modern physics, Hume was well known for his skeptical elimination of the concept of necessity from causality, that is, for claiming that the only basis for a causal relation between two events is simply the mind's perception that the events are repeatedly (or constantly) conjoined. Hume converted the objective regularity between events into a subjective (representationalist) experience. For Hume, there is no causality apart from the perception of events that are strictly correlated in time. Kant, in a stunning foreshadowing of modern perceptual neuroscience, argued that causality is a synthetic *a priori* judgment. According to Kant, mental representations, including causality, are not simply reflections of the world, but are categories of understanding used to actively interpret events in the world. The implication is that causality need not be determined by external events. Going even further, Bertrand Russell argued that modern science has demonstrated that causality need not be intrinsically tied to determinism. Thus, since the time of Russell, a distinction is made between deterministic causality and probabilistic causality. As we shall see, motivations for probabilistic theories of causality stem from difficulties with so-called regularity theories, which originate in Hume's idea of constant conjunctions.

This review considers the proposition that probabilistic causality is well suited for understanding causal influences in the brain, where bi-directional and convergent pathways play a major role in processing. Such complex organizational features of brain connectivity imply that interaction models based on linear transmission from unitary senders to unitary receivers are too rigid. The first half of the review consists of a discussion of classical notions of causality,

[1] This paper discusses neural causality at the level of neuronal populations because it is the neuronal population that is thought to represent the unit of interaction in large-scale brain networks, whose operations are proposed to underlie cognition in the brain (see [56]). Neural causality may also apply to the interactions of individual neurons within a population wherever a similar connectional topology prevails at the single-neuron level.