What is the nature of causality in the brain? - Inherently probabilistic. Comment on “Foundational Perspectives on Causality in Large-Scale Brain Networks” by M. Mannino and S. L. Bressler

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Understanding cause-and-effect (causal) relations from observations concerns all sciences including neuroscience. Appropriately defining causality and its nature, though, has been a topic of active discussion for philosophers and scientists for centuries. Although brain research, particularly functional neuroimaging research, is now moving rapidly beyond identification of brain regional activations towards uncovering causal relations between regions, the nature of causality has not been thoroughly described and resolved. In the current review article [1], Mannino and Bressler take us on a beautiful journey into the history of the work on causality and make a well-reasoned argument that the causality in the brain is inherently probabilistic. This notion is consistent with brain anatomy and functions, and is also inclusive of deterministic cases of inputs leading to outputs in the brain.

A living brain is a complex dynamical system with many highly interconnected, interacting and self-organizing entities (neurons). The traditional notion of brain regions as information-processing units, with an input, a local-processing capability and an output is too rigid and is not generally applicable throughout the brain. An ultimate response of a neuronal system in the brain is determined by feedforward, feedback and modulatory influences and is not always guaranteed [2]. Incoming inputs, even in absence of neuronal outputs, can bring about other physiological changes such as local cerebral blood flow changes [3]. In view of a likelihood of an observable neuronal response in an ongoing stream of various inputs, probabilistic causality is more appropriate for describing neural influences. Granger causality measures in both time- and frequency-domains [4, 5] and with estimation approaches based on either autoregressive modeling [6] or spectral factorization [7, 8] are consistent with the probabilistic notion of causality. These measures have been applied to study causal relations in large-scale brain networks from a variety of brain function recordings, including local field potentials (LFPs), electroencephalography (EEG), magnetoencephalography (MEG), and functional magnetic resonance imaging (fMRI) [9, 10, 11], functional near-infrared imaging [12], intra-cortical EEG [13].

This review [1] also makes an excellent distinction between Granger causality and dynamical causal modeling (DCM) [14], another widely used method to study causal relations among regions of large-scale networks. The original DCM [14] relies on deterministic models of distributed neuronal responses (often hidden) to external inputs to the brain due to sensory stimulation or task performance. This version of DCM treats the brain as a deterministic dynamical system and causal relations obtained are based on neuronal input to output relations. The causal relations thus obtained are deterministic in nature. A recent version usually referred as stochastic DCM (sDCM) [15, 16], however, uses modeling of stochastic dynamical systems

to describe hidden variables generating the observed brain data in situations of no explicit tasks or sensory stimulation. This version of DCM can allow for a probabilistic interpretation of causality.

The human brain is considered to be one of the most complex systems in the universe. There are many mysteries to be solved including the patterns of causal relations among brain regions during perception, cognition and behavior. This review [1] comes in a right time when a major initiative like the BRAIN initiative is underway in attempt to mapping the entire human brain. These perspectives on the nature of causality relating to the brain in the review are helpful for identifying and using the appropriate network activity analysis tools for these and other similar efforts.

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