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Review

The use of functional and effective connectivity techniques to understand the developing brain

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ABSTRACT

Developmental neuroscience, the study of the processes that shape and reshape the maturing brain, is a growing field still in its nascent stages. The developmental application of functional and effective connectivity techniques, which are tools that measure the interactions between elements of the brain, has revealed insight to the developing brain as a complex system. However, this insight is granted in discrete windows of consecutive time. The current review uses dynamic systems theory as a conceptual framework to understand how functional and effective connectivity tools may be used in conjunction to capture the dynamic process of change that occurs with development.

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1. Introduction

The brain is a complex and dynamic functional system, characterized by constant activity and change. Billions of neurons form intricate patterns that can flexibly integrate based on shared function, forming networks that are constrained by, but not limited to, direct structural connections of the brain (Vincent et al., 2007). Functional networks have the amassed capacity to support complex thought and action that any single element of the system would be unable to support alone. However, the topology of functional networks has been largely intangible until the relatively recent emergence of functional and effective connectivity techniques. Respectively, these tools measure the temporal correlation between remote neurophysiological events (Sporns et al., 2007) and the influence one neural system exerts over another (Friston, 2009). Together, functional and effective connectivity techniques have provided remarkable insight to the brain as a set of interconnected elements embedded within a larger whole.

Increasingly, researchers in the field of developmental cognitive neuroscience are implementing connectivity techniques, making methodological and conceptual strides in the understanding of the developing brain (e.g., Fair et al., 2007, 2008; Dosenbach et al., 2010). These studies have revealed that the complex functional architecture of the brain changes throughout the lifespan. Specifically, functional brain networks in children appear to be composed of multiple decentralized clusters at the local level, while adult function is supported by a more integrated organization distributed throughout the brain (for review, see Vogel et al., 2010). To contribute to this burgeoning literature, the present review summarizes and synthesizes developmental research implementing connectivity techniques to understand the emergence of networks in the brain. In other words, how might mature patterns of connectivity arise as a developmental product of precursors that did not contain these patterns? A dynamic systems framework may provide valuable theoretical principles for conceptualizing the complex interrelations of physical form, time, and process that contribute to the emergence of networks in the human brain.

Dynamic systems theory has been referred to as the broadest and most encompassing of all the developmental theories (Miller, 2002). As defined in the present review, *dynamic systems* is a theoretical approach that describes the behavior of complex networks (Smith and Thelen, 2003). This is different from the more technical use of the term, *dynamical systems*, which refers to a class of mathematical equations that describe time-based systems with particular properties (e.g., Luenberger, 1979). The qualitative principles of this approach are content-independent and have been previously applied to a range of developmental questions such as language acquisition (De Bot et al., 2007), emotion (Lewis and Granic, 2002), and cognition (Thelen, 1996), though have not yet been widely applied to questions of neurobiological development. Under dynamic systems theory, development can only be understood as the multiple, mutual, and continuous interaction of all levels of the developing system. This concept singularly resonates with the growing understanding of the brain as an interconnected system, a series of simpler networks organized into increasingly complex networks, undergoing a changing trajectory throughout the lifespan (Power et al., 2010). The application of this theory to understand the developing brain may help answer such questions as: How can the stable and integrated pattern of the adult neural network emerge from the decentralized patterning typical of a child's brain? How can the local community clusters of a child's brain emerge from a single neuron communicating to another? According to dynamic systems theory, the key to understanding these fundamental developmental questions lies within the process of self-organization. Some form of global order or coordination arises out of the local interactions between the components of an initially disordered system. In other words, development of networks may organically emerge as a product of the system's own activity and the *relationship* between the system's component parts. Connectivity techniques provide a set of tools for researchers to examine *interactions* between elements of the brain. The current review describes tools to assess functional and effective connectivity and describes a framework for understanding large-scale networks. Although the tools described here do not represent the entirety of available techniques implemented to evaluate functional and effective connectivity, they are widely used and have been selected to demonstrate the power of these approaches thematically. Individually and together, these tools have the potential to offer significant contribution in the methodological and conceptual strides being made toward an understanding of the developing brain as a dynamic system. The reader is directed to reviews discussing methods not discussed here, such as Granger causality (Friston et al., 2013).

The general principles of dynamic systems theory may be useful for conceptualizing biological self-organization. The first such principle is the tenet of multicausality, which assumes that the regularities of the mature organism patently emerge from multiple factors, including internal configuration of the system and external changes in the environment that the system responds to. The stable and distributed functional system of the mature brain may be a developmental product of multiple sources, including the system's internal configuration (i.e., intrinsic architecture) and its response to the external environment (i.e., extrinsic architecture). The brain's intrinsic architecture is defined as the spontaneous fluctuations between elements of the neural system in the absence of an explicit task, which can be assessed through the acquisition of functional data such as resting-state. This intrinsic architecture may provide a framework for the moment-to-moment responses that the external world evokes (Fox and Raichle, 2007; Raichle, 2010). Extrinsic networks, defined as in-the-moment coupling of regions in response to external stimuli, may be assessed through task-evoked effective connectivity techniques, such as dynamic causal modeling (DCM). Individually and together, the intrinsic and extrinsic architectures of the brain have the potential to shape the development of functional networks through a shared history of co-activation. Through the use of functional and effective connectivity techniques, researchers can better understand the multiple influences on a developing