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Brain connectivity: an opening window into addiction

Vince D Calhoun^{1,2}

¹The Mind Research Network, Albuquerque, New Mexico 87131

²Dept. of ECE, University of New Mexico, Albuquerque, New Mexico

Almost twenty years ago, brain connectivity based on brain imaging data (or alternatively, mapping of the macro-connectome) was introduced to the field¹. Since then we have learned a lot about methodology, imaging approaches, and brain health and disease using approaches based on connectivity. Approaches range from univariate correlation between targeted regions of interest¹ to data-driven multivariate approaches like group independent component analysis². In this commentary I touch on three topics: 1) the prevalence of studies of connectivity in the area of substance use disorders, 2) the information brain connectivity can provide us, and 3) some future directions in brain connectivity.

Studies of brain connectivity, growing, yet lagging in addiction-related areas

This special issue presents a series of articles focused on how functional and structural connectivity change in the context of addiction. This is extremely important given the widespread impact of substance use disorders on our daily lives, as well as the interaction among substance use and mental health. There are a growing number of studies of brain connectivity applied to addiction-related topics, it appears that in the general area of substance use, studies of brain connectivity appear to be lagging behind other brain-based disorders. A PubMed search comparing several other disciplines with various combinations of brain connectivity and substance use-related measures reveals that the number of studies of addiction and substance use are on the lower in terms of a focus on brain connectivity as a measure of interest (see Figure 1). It is especially concerning to see topics like impulsivity, and even reward, having so few studies, especially given the NIMH Research Domains Criteria (RDoCs) in which a focus away from symptom-based measures towards biologically based biomarkers of mental illness are encouraged³. Cognitive constructs like impulsivity, reward, and many others which are related to substance use will likely play a key role in untangling how the brain functions in health and dysfunctions in disease.

Brain connectivity provides unique information

One of the reasons brain connectivity studies are important as they provide information that traditional voxel-wise task-based regression analysis do not. For example, with brain connectivity you can identify networks responding to a task, in slightly different ways,

whereas these would likely get grouped together in a task-based regression approach. In addition, brain connectivity studies can help identify coherent sets of voxels (i.e. networks) that are present either at rest or task. A major advantage of functional brain connectivity studies is the can identify resting networks and compare these with networks during a task, unlike a typical task-based regression approach which often treats rest activity as a type of baseline. There are widespread methods for studying connectivity, as is clear from the papers represented in the special issue. For functional connectivity seed-based and independent component analysis-based approaches are perhaps the most widely used, complementary to one another but with different strengths and limitations⁴. Brain connectivity studies also enable one to analyze the temporal information within each connectivity network, there are many ways to do this from comparing with a task, analyzing spectral content (as in the amplitude of low frequency fluctuation approach) and incorporation correlation or graph-based measures to look for inter-relationships between connectivity networks.

Future directions

Brain connectivity approaches, though widespread, are still in a relatively early phase of development. There are currently many exciting new directions in the analysis of brain connectivity. These include the analysis of dynamic changes (i.e. the identification of connectivity states emerging and subsiding at different times) which seems a more natural way to analyze task and especially resting data given its rather uncontrolled and dynamic nature^{5, 6}. Methods of studying the relationship between structural and functional connectivity are also rapidly growing, as it is well known that brain structure serves as a substrate for brain function. Graph-based methods, widely used in other fields, are becoming more common in the brain imaging field and can provide a high-level way to summarize the complex information contained in BC studies⁷ in both health and disease. In addition, multimodal analysis methods can provide new information about the complex inter-relationship of brain structure and function which are not detectable by working with one imaging modality alone⁸. It is only a matter of time before studies of addition will utilize these and other approaches.

In conclusion, as the articles in this special issue and as the introduction to the special issue highlights, the study of functional and structural brain connectivity in the context of addiction is a highly useful approach which, though initially lagging behind other fields, is starting to accelerate. Brain imaging is limited by many factors, most notably it provides a macroscopic view of a highly complex system. It is only by bringing together the many imaging modalities, experimental designs, analytic methods, and conceptual models that we can identify and weave together the relevant information for understanding the brain and its dysfunction.

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Figure 1.

Addiction and Substance use studies focused on brain connectivity are lagging behind studies of mental illness such as autism and schizophrenia.