

# High Temporal Resolution Measurement of Cognitive and Affective Processes in Psychopathology: What Electroencephalography and Magnetoencephalography Can Tell Us About Mental Illness

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As the field of cognitive neuroscience matures, increasing emphasis has been placed on understanding the brain in the context of networks, rather than as isolated structures or independent neurotransmitter systems. These networks operate on rapid time scales to produce flexible, adaptive mental processes in neurotypical individuals, and abnormalities in the operation of these networks can play a significant role in mental illness. Because these networks often operate on a scale of tens or hundreds of milliseconds, neural recording techniques with high temporal resolution, such as electroencephalography (EEG) and magnetoencephalography, are critical for disentangling and deciphering the many individual processes that underlie psychological dysfunction.

Though limited in some ways by their comparatively poor spatial resolution, EEG and magnetoencephalography permit the parsing of cognitive events that might otherwise be indistinguishable using techniques with high spatial resolution, such as functional magnetic resonance imaging. For example, ordinary language comprehension often involves hearing two to four words per second, and each word therefore needs to be parsed, recognized, and integrated with the rest of the sentence in a fraction of a second. EEG and magnetoencephalography are well suited for isolating these specific processes and determining which processes are impaired in a given diagnostic group. For example, Kuperberg *et al.* (1) used event-related potentials (ERPs) extracted from EEG recordings to isolate two distinct stages of referential processing, one that was impaired in people with schizophrenia and one that was relatively preserved. Thus, high temporal resolution recording methods can yield critical insights into how specific cognitive processes that support language comprehension can fail in mental illness.

In this special issue of *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging*, we highlight the multiple ways in which classical and cutting-edge high temporal resolution recording and analysis techniques can be used to probe physiological mechanisms of psychopathology in a dimensional and transdiagnostic way. In recent years, there has been broad acknowledgement that traditional approaches to studying mental illness based on discrete diagnostic categories has limited our understanding of the relationship between pathophysiology and abnormal behavior. The Research Domain Criteria initiative (2) represents one attempt to shift

research away from diagnostic classifications and toward identifying common neurobehavioral constructs that give rise to shared symptom features across psychiatric illnesses. Such a shift in conceptualization may yield more fruitful approaches to understanding the relationship between altered physiological processes and psychopathology.

In the present issue, the use of high temporal resolution recordings to assess construct domains across diagnostic boundaries is discussed at length in a review by Klumpp and Shankman (3). These authors highlight the significant comorbidity and heterogeneity that exists between and within anxiety and depressive disorders in the general population, and posit that this suggests the existence of clinically meaningful transdiagnostic subgroups characterized by shared neurobiological mechanisms. For example, either depression or anxiety may result from disruption in one or more subconstructs within either the negative valence system (e.g., heightened sensitivity to potential threat or nonreward) or the positive valence system (e.g., reduced responsiveness to reward). Importantly, high temporal resolution methodologies are ideally suited for parsing these cognitive events that occur rapidly after the presentation of a rewarding or threatening stimulus. Klumpp and Shankman (3) review evidence that heightened startle reactivity (reflecting increased response to threat) may be a useful distinction between fear-based manifestations of anxiety and anxiety that is predominantly characterized by distress-misery. Similarly, the presence or absence of blunted positive valence responses after the presentation of pleasant stimuli may be a meaningful distinction between primarily anxious and primarily depressed individuals.

In keeping with this conceptualization, Weinberg and Sandre (4) used EEG to identify contributions of negative and positive valence processes in a large sample of individuals characterized by varying levels of positive and negative affect. The authors found that low positive affect was associated with blunted responses to reward and threatening stimuli, whereas high fear-based negative affect was associated with heightened attention at early stages of visual perception. Thus, these approaches to identifying clinically meaningful subgroups within the internalizing disorders spectrum represent a fruitful strategy that advances our collective understanding of the etiological factors at play in the development of mental illness.

Whereas the above studies show the utility of traditional analysis applications of high temporal resolution data for identifying neural mechanisms of symptom expression, continued development of sophisticated analysis techniques has expanded the range of questions that these methodologies can be used to answer. For example, time-frequency analysis techniques allow for testing hypotheses about not only when a cognitive event occurs, but also how. Specifically, these techniques can be used to isolate neural oscillations in different frequency bands that reflect different kinds of underlying networks and play distinct roles in psychological phenomena such as attention and memory. Findings of abnormalities in these oscillatory signals can provide important clues about the nature of the neural network disruptions that underlie psychiatric disorders such as attention-deficit/hyperactivity disorder (5).

Related techniques that incorporate time-frequency analysis can also be used to understand communication within large-scale neural networks in health and illness. Whitton *et al.* (6) examined functional connectivity between nodes within the default mode and frontoparietal networks in a large sample of healthy individuals and individuals with major depressive disorder. These authors reconstructed cortical activity at different nodes within these two networks from resting-state EEG and found evidence for hyperconnectivity within and between networks among individuals with major depressive disorder. Furthermore, the magnitude of functional connectivity within the beta frequency band was significantly associated with clinical severity. In another study using time-frequency analyses to quantify resting-state EEG signals, Hirano *et al.* (7) report evidence for abnormal phase-amplitude coupling—the degree to which the amplitude of higher oscillation frequencies is modulated by the phase of lower oscillation frequencies—in a sample of people with schizophrenia. Although the clinical significance of these disturbances as they relate to symptom profiles and abnormal cognition is only just beginning to be understood, the expanded use of such methodology may yield novel areas of exploration to account for the relationship between these forms of network disruption and symptoms of psychopathology.

Finally, altered physiological processes captured by high temporal resolution recording methods may also reveal a vulnerability to mental illness and/or markers of relapse risk that are present even in the absence of overt cognitive and affective disruption. Nelson *et al.* (8) assessed EEG during a monetary guessing task using both traditional ERP measures and time-frequency analyses in a large sample of teenage girls, some of whom later developed a diagnosis of major depressive disorder. These authors found that blunted ERPs and delta-oscillation responses to monetary reward each contributed significant, independent variance to the prediction of a depressive disorder during the 18-month follow-up period. Thus, trait-like automatic reward responsivity is implicated as a clinically meaningful mechanism by which depression emerges in a subset of individuals—even though overt mood and associated cognitive processes are not yet disrupted. Similarly, Houston and Schliez (9) review the use of high temporal resolution indices as biomarkers for vulnerability to future relapse among individuals with substance use disorders who are currently abstinent. These authors report that early

attentional responses to neutral and substance-related visual cues serve as important predictors of future substance use, despite current abstinence. Altogether, this work highlights the importance of trait-like differences in early cognitive processes that lend insights into neurobiological mechanisms of risk and relapse in mental illness.

The articles featured in the present issue of *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging* highlight the many ways in which novel and innovative approaches to high temporal resolution data analysis can be used to understand the neural mechanisms of cognitive and mood disruption across a variety of mental illnesses. These methodologies have the advantage of 1) being able to measure neural activity as it unfolds in real time during cognitive tasks and at rest, and 2) being easily acquired from individuals across the lifespan—including infants—to track the development and progression of disorders that emerge early in development (10). From innovative use of traditional ERP analysis techniques (1,4) to time-frequency analysis (5,7,8) and the use of source reconstruction to examine oscillatory properties of functional networks (6), recent expansion of the range of high temporal resolution recording methods has opened up new avenues for understanding the pathophysiology of mental illness.

### Acknowledgments and Disclosures

The authors report no biomedical financial interests or potential conflicts of interest.

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Received Nov 28, 2017; revised Nov 28, 2017; accepted Nov 29, 2017.

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