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HOT TOPICS

Densely sampled neuroimaging for maximizing clinical insight in psychiatric and addiction disorders

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To overcome limitations with neuroimaging work in small clinical samples, large-scale data collection and data pooling initiatives have been established and are ongoing. These "big data" initiatives aim to maximize sample size and are anticipated to transform our neurobiological understanding of psychiatric disorders. A complementary—yet much less appreciated in the context of clinical neuroimaging—form of big data is the acquisition of large amounts of data over time for a small(er) number of individuals, or *dense sampling*. We argue such dense sampling of neuroimaging data is needed in psychiatry to provide essential information about the neurobiological foundations of what are highly dynamic disorders of brain function. As with densely sampled psychological data [1, 2], tying densely sampled neuroimaging data collection to clinically meaningful transitions, such as standard phases of clinical care of an individual, can, we suggest, help maximize mechanistic insight and lead to improved translation of findings to treatment development, as highlighted here within the specific context of addiction.

While informative and efficient, the necessary focus of case-control studies on static, group-average deviations from a presumed "normative" population may preclude their real-world clinical utility. For example, recent machine learning studies of addictions indicate that brain networks which distinguish patients from controls are often distinct from those that predict specific clinical outcomes within-group [3, 4]. This striking distinction suggests person-specific neurobiology is dissociable from group-specific patterns; as such, group-specific findings may not translate to improved understanding of person-specific pathophysiology or to treatment.

Unlike case-control designs, treatment-oriented neuroimaging studies seek to characterize neurobiology among patients entering treatment with the aim of identifying individual brain-based markers of clinical outcomes [3, 4]. However, this approach may still be limited. As illustrated in Fig. 1, recovery from addiction can take months to years and clinical trajectories vary widely across individuals. In addition, gold-standard treatments, such as medications for opioid use disorder or types of behavioral therapies, are multiphasic, requiring continuous adjustment based on an individual's current needs. Complete understanding of addiction neurobiology, and translation of this understanding to clinical care, will thus likely require repeated neuroimaging such as that afforded by dense sampling.

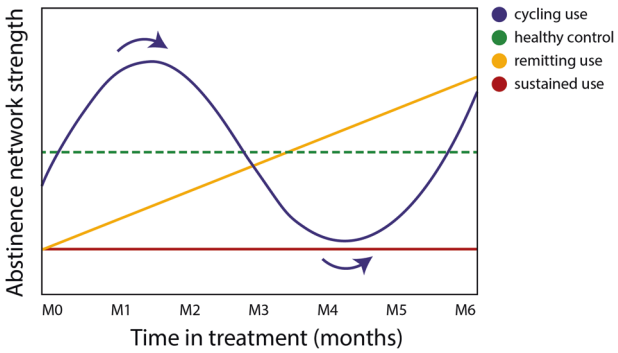

Fig. 1 Prognosis-based classification of individuals based on the strength of their "abstinence network" over 6 months of treatment initiation. Evolution of the strength of an individual's abstinence network (set of functional brain connections predictive of lowered risk for future substance use [3, 4]) as captured by densely sampled neuroimaging data acquisition (~bi-weekly over 6 months). The example cases represent realistic trajectories: (1) healthy/control, shown to remain at moderate network strength over time; (2) sustained use, also shown to remain stable over time but at a low-abstinence network strength; (3) cycling use, shown to move away from an initial low-abstinence starting point and then start to return to it. Here we also highlight at what time points tailored treatment, such as additional psychosocial support or medication adjustment, might be most efficacious (i.e., when individuals might be most susceptible to intervention strategies) designated by the solid arrows; and (4) remitting use, also shown to change over time but in a single direction approaching health/high-abstinence network strength.

Although representing a paradigm shift for clinical neuroimaging, dense sampling of neuroimaging data is already a core part of basic research in human neuroscience [5]. These studies span those that measure the dynamic substrates of complex cognitive function and brain network organization—both of relevance to psychiatry—and that sample at a frequency as short as a day and for a duration as long as a full year. Such dense sampling work has demonstrated, for example, functional brain changes <48 h of a clinical intervention (wearing a cast) that quickly reverse following treatment cessation (cast removal) [6]. It is likely that similar, clinically-meaningful, neural changes occur with psychiatric interventions, and as an individual progresses towards or away from

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successful recovery. Using dense sampling to understand addiction pathophysiology at multiple levels and timescales promises to meet the challenge of modern psychiatry and to bring neuroimaging to bear on its ultimate goal—informing clinical care.

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AUTHOR CONTRIBUTIONS

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COMPETING INTERESTS

The authors declare no competing interests.

ADDITIONAL INFORMATION

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