fMRI-based Biomarkers for
Multiple Components of Pain

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Objective biomarkers of pathology exist for a number of diseases, and their development is one of the great advances of modern allopathic medicine. However, objective assessment of pain and other mental health disorders has lagged far behind. Pain cannot be explained by peripheral damage alone; it is caused by a variety of neuropathological processes, which has made it difficult to assess and treat. Currently, the only acceptable way to measure pain is by self-report, which presents a serious barrier to effective research and treatment. Self-reported pain is influenced by nociceptive, affective, and cognitive decision-making processes-and though there are many treatments that can influence reported pain, they likely do so through a heterogeneous set of neurophysiological mechanisms, with different consequences for health and long-term well being. As a result, in spite of a long history of research, current treatments for pain are effective for a minority of individuals, with enormous costs to patients and to society. Biomarkers for physical pain could dramatically improve diagnosis and treatment, by allowing pain to be characterized on the basis of underlying neuropathology, rather than external symptoms. They could also improve treatment, by allowing interventions to be targeted to type of neuropathology involved. Biomarkers that can shed light on the brain pathophysiology that causes pain must necessarily rely on direct measures of brain function. In the past several years, major advances in combining functional magnetic resonance imaging (fMRI) with machine learning techniques-algorithms for finding predictive patterns in complex datasets-have brought the goal of fMRI-based pain assessment within reach. In preliminary data, we show for the first time that fMRI activity can predict whether an individual person is experiencing high or low physical pain with over 90% sensitivity and specificity. Critically, the biomarker is specific to physical pain when compared with non-painful touch and several classes of salient, affective events. In addition, it achieves this level of accuracy when applied prospectively to new samples, across different scanners and paradigms. This preliminary success raises a number of issues that must be addressed before fMRI-based biomarkers can be used in large-scale clinical trials and clinical practice, including a) robustnes across laboratories and procedures, b) specificity to body site, modality, and quality of pain, c) responses to analgesic treatment, and d) applicability to spontaneous and acute hypersensitivity/allodynia in clinical populations. Here, we propose to aggregate existing data across a consortium of researchers, allowing more extensive tests of sensitivity and specificity across 13 fMRI studies in healthy individuals and 18 studies in diverse clinical pain populations. In addition, we will conduct five new experiments to address critical aspects of biomarker performance. These data will allow us to develop and validate new, more comprehensive biomarkers that can assess multiple aspects of pain across healthy individuals and chronic pain sufferers. PUBLIC HEALTH RELEVANCE: Pain affects nearly everyone at some time in their lives, with enormous costs to individuals and society. Current treatments for pain are only modestly effective, in large part because pain is created through a complex set of brain processes and can be measured only by patients' self-reports, which presents a serious barrier to effective research and treatment. This project capitalizes on recent breakthroughs in measuring human brain activity and using it to objectively assess the brain processes that underlie pain experience, which could transform the way pain is measured and new treatments are developed.