Detecting the psychosis prodrome across high-risk populations using neuroanatomical biomarkers

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To date, the MRI-based individualized prediction of psychosis has only been demonstrated in single-site studies. It remains unclear if MRI biomarkers generalize across different centers and MR scanners and represent accurate surrogates of the risk for developing this devastating illness. Therefore, we assessed whether a MRI-based prediction system identified patients with a later disease transition among 73 clinically defined high-risk persons recruited at two different early recognition centers. Prognostic performance was measured using cross-validation, independent test validation, and Kaplan-Meier survival analysis. Transition outcomes were correctly predicted in 80% of test cases (sensitivity: 76%, specificity: 85%, positive likelihood ratio: 5.1). Thus, given a 54-month transition risk of 45% across both centers, MRI-based predictors provided a 36%-increase of prognostic certainty. After stratifying individuals into low-, intermediate-, and high-risk groups using the predictor's decision score, the high- vs low-risk groups had median psychosis-free survival times of 5 vs 51 months and transition rates of 88% vs 8%. The predictor's decision function involved gray matter volume alterations in prefrontal, perisylvian, and subcortical structures. Our results support the existence of a cross-center neuroanatomical signature of emerging psychosis enabling individualized risk staging across different high-risk populations. Supplementary results revealed that (1) potentially confounding between-site differences were effectively mitigated using statistical correction methods, and (2) the detection of the prodromal signature considerably depended on the available sample sizes. These observations pave the way for future multicenter studies, which may ultimately facilitate the neurobiological refinement of risk criteria and personalized preventive therapies based on individualized risk profiling tools.
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