Trajectories of Psychiatric Disorders and the Challenge of Relapse and Recurrence: A Network Perspective

Andrew A. Nierenberg, MD

The long-term, real-world trajectories of people with psychiatric disorders, including schizophrenia, major depressive disorder, and bipolar disorder, all too often consist of repeated episodes of illness (relapses or recurrences) or persistent symptoms and disability.[1-3] Why? I could glibly state that the predictors associated with poor trajectories are multi-determined—early age of onset, childhood adversity, more severe illness, comorbid conditions, psychosocial stress, lack of supportive relationships or stable housing, or not taking medications or attending psychotherapy optimally. In some ways, the usual list of suspects that predict a poor trajectory across diagnoses could be interpreted as simply, the sicker one is, the sicker one will continue—a trivial relationship that Ron Kessler, PhD (McNeil Family Professor of Health Care Policy, Department of Health Care Policy, Harvard Medical School) taught me during one of our collaborations analyzing data. There is just something not satisfying about thinking of poor trajectories this way and it does not lead to solutions.

Instead, indulge me as I try to wrestle with finding a more satisfying explanation. First, of course, we do not yet have a complete enough understanding of the psychiatric pathophysiology and therefore our treatments may fail to target dysregulations in any person. But what if we did have specific targets? Would we, and could we cure psychiatric disorders? Shouldn't such targeted treatment lead to a cure? Loscalzo invokes the mathematical properties of biological networks and their tendency to respond to perturbations initially and then revert back to pre-treatment configurations.[4,5] This helps me to reconceptualize the effect of treatment (ie, any given target is embedded within a network and hitting that target will lead to an incomplete change in the network, optimally moving from the "diseaseome" closer to the "healthome").[6,7] The trick is to lock the network into the "healthome" by changing the "interactome." This network understanding is probably why many patients need multi-modal treatments, especially psychotherapy and psychopharmacology. Additionally, this network understanding helps me realize that we are inappropriately using the metaphor of infectious disease (hit the target, kill the bug, cure). As our field evolves, network analyses may help us not only understand the suboptimal trajectories of psychiatric disorders, but also find network solutions for better long-term outcomes.[8]

Andrew A. Nierenberg, MD, is the Thomas P. Hackett, MD, Endowed Chair in Psychiatry, the Director of the Dauten Family Center for Bipolar Treatment Innovation, and the Co-Director, Center for Clinical Research Education, Massachusetts General Hospital; and a Professor of Psychiatry, Harvard Medical School.

Address correspondence to Andrew A. Nierenberg, MD, via email: psyann@Healio.com.

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