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Title: Psychosis in Neurodegeneration: Relating Phenomenology to Pathology and Prognosis

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Psychosis is a uniquely disabling complication of several neurodegenerative diseases. In recent years, it has emerged as the focus of an increasing number of clinical investigations, approached from both pathological and phenomenological perspectives in several disease-specific contexts. One might imagine an eventual paradigmatic conception of psychosis that explicates its mechanistic underpinnings across multiple diseases. This is likely to be overly simplistic, given the heterogeneous nature of the symptoms that are often classified under the heading of psychosis, as well as the complexity of networks involved in generating perceptions and beliefs that are not congruent with reality. Recent work has reinvigorated the dopamine hypothesis of psychosis in schizophrenia and bipolar affective disorder,[1] but it seems to us unlikely that the forms of psychotic phenomena that appear in neurodegenerative disorders possess significant mechanistic or pathologic overlap with such Kraepelian psychoses. Nonetheless, it is striking and certainly non-trivial that such fundamentally different organic disorders can produce ostensibly comparable disturbances of perception and belief.

This commonality acknowledged, it is also important to note that failure to recognize the diversity of psychotic phenomena in research settings—even within the context of a single primary disease state—has perhaps hampered progress in defining biological origins. In the