Is psychosis toxic to the brain?

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Schizophrenia has been described as the "worst disease" to afflict mankind.[1] It causes psychosis, which is an abnormal state of mind marked by hyperarousal, overactivation of brain circuits, and emotional distress. An untreated episode of psychosis can result in structural brain damage due to neurotoxicity. Patients who experience psychosis may be affected by inflammatory processes, oxidative and nitrosative reactions, mitochondrial dysfunction, decreased synaptic plasticity and neurogenesis, demyelination, and autoimmune attacks—all of which can contribute to cell necrosis and irreversible neuronal atrophy.[2-4]

The impacts of untreated psychosis

First-episode psychosis (FEP) can result in a loss of up to 1% of total brain volume and up to 3% of cortical gray matter.[4,5] When FEP goes untreated, approximately 10 to 12 cc of brain tissue—basically a tablespoon of cells and myelin—could be permanently damaged.[2,6,7] This explains why enlarged ventricles are a common radiologic finding in patients with schizophrenia.[2] In such patients, imaging of the brain will show these as hollow, fluid-filled spaces that appear expanded.

Repeated episodes of untreated psychosis could result in progressively lower levels of baseline functioning, and patients may require longer hospitalizations to achieve stabilization and higher doses of medications to achieve remission.[4,7] Greater brain volume losses are associated with poorer outcomes.[3] Brain volume loss is also detectable in patients with untreated major depressive episodes,[8] and recurrent episodes of bipolar I disorder can also result in the loss of gray matter and structural brain damage.[9] The progressive decline in cognitive and functional outcomes and eventual development of treatment resistance are likely due to a kindling phenomenon or receptor sensitization.[10]

Act fast to prevent brain damage

Since it was first identified, schizophrenia has been recognized as a degenerative disease. However, the progression to structural brain damage is not inevitable, and can be arrested with expeditious, decisive treatment. Some agents, such as certain antipsychotic medications[10] and omega-3 fatty acids, can be neuroprotective.[11] The early use of a long-acting injectable antipsychotic also may help prevent relapse and additional psychotic episodes.[5]

Psychosis requires expedient and competent intervention to improve outcomes and reduce disease burden. Timely psychiatric treatment can improve not only immediate functioning, but also long-term prognosis. Because untreated psychosis can result in irreversible structural brain

damage, clinicians must act swiftly to provide assertive treatment.

References

1. Where next with psychiatric illness? Nature. 1998; 336(6195):95-96.
2. Salisbury DF, Kuroki N, Kasai K, et al. Progressive and interrelated functional and structural evidence of post-onset brain reduction in schizophrenia. Arch Gen Psychiatry. 2007;64(5):521-529.
3. van Haren NE, Hulshoff HE, Shnack HG, et al. Progressive brain volume loss in schizophrenia over the course of the illness: evidence of maturational abnormalities in early adulthood. Biol Psychiatry. 2008;63(1):106-113.
4. Cahn W, Hulshoff Pol HE, Lems EB, et al. Brain volume changes in first-episode schizophrenia: a 1-year follow-up study. Arch Gen Psychiatry. 2002;59(11):1002-1010.
5. Subotnik KL, Casaus LR, Ventura J, et al. Long-acting injectable risperidone for relapse prevention and control of breakthrough symptoms after a recent first episode of schizophrenia. a randomized clinical trial. JAMA Psychiatry. 2015;72(8):822-829.
6. Nasrallah HA. FAST and RAPID: acronyms to prevent brain damage in stroke and psychosis. Current Psychiatry. 2018;17(8):6-8.
7. Nasrallah HA. For first-episode psychosis, psychiatrists should behave like cardiologists. Current Psychiatry. 2017;16(8):4-7.
8. Moylan S, Maes M, Wray NR, et al. The neuroprogressive nature of major depressive disorder: pathways to disease evolution and resistance, and therapeutic implications. Mol Psychiatry. 2013;18(5):595-606.
9. Kozicky JM, McGirr A, Bond DJ, et al. Neuroprogression and episode recurrence in bipolar I disorder: a study of gray matter volume changes in first-episode mania and association with clinical outcome. Bipolar Disord. 2016;18(6):511-519.
10. Chen AT, Nasrallah HA. Neuroprotective effects of the second generation antipsychotics. Schizophr Res. 2019;208:1-7.
11. Amminger GP, Schäfer MR, Schlögelhofer M, et al. Longer-term outcome in the prevention of psychotic disorders by the Vienna omega-3 study. Nat Commun. 2015;6:7934. doi: 10.1038/ncomms8934.

Certain antipsychotic medications and omega-3 fatty acids can be neuroprotective