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# Did My Eighth Grade Girlfriend's Dad Cause My Psychosis?

*A Brain in Flames*

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I survived childhood sexual abuse. Three different times, by three different adults, within two years. In my second year of college, I developed psychosis during finals week, took emergency incompletes on all of my classes, and was later diagnosed with schizoaffective, depressive type: a combination of schizophrenia and major depression. Notice that I didn't say schizoaffective disorder, nor major depression disorder, as they are officially titled. I dislike these words. I say diff-order, because I have order, but it's certainly different from yours (unless you have a schizophrenia spectrum difforder too, in which case send me an email!).

What is schizophrenia? It's a brain abnormality that results in being out of touch with our shared reality. Contrary to popular belief, it does not include multiple personalities, nor does it cause people to become violent. Schizophrenia is characterized by hallucinations, which often take the form of hearing voices that aren't there, having visions that others can't see, and feeling feelings, and rarely smelling smells, that don't exist in our shared reality. I hear voices that make me turn my head, and I have seen giant looming faces on each wall of my room and assassins in all black watching me from my doorway. Even as I sleep, I may feel a thousand bee stings or ants crawling up and down each of my legs.

Schizophrenia also includes delusions, which are fixed beliefs that don't initially respond to reasoning. For example, I used to have delusions that my family were about to assault me sexually—I still hear voices saying these horrors will happen soon. Other symptoms include flat affect, apathy, "poverty" of thought, and disrupted speech. But why? Some major findings support a hypothesis that starts with inflammation.

We all know about inflammation from personal experience. If you get a bug bite or a broken bone, the affected body part swells a little or a lot. This reaction is called an immune response. It turns out that traumatic emotional stress can also lead to inflammation, this time in the brain. Cerebral inflammation is associated with a number of inflictions, including schizophrenia.

One model by Miller, Chen, and Parker in 2011 suggests that if intense stress occurs during brain development, when the brain is highly plastic, the stress-induced inflammation can stick around far after the initial incident. More precisely, inflammation markers rise to chronically high levels in some adults who experienced childhood maltreatment (CM), which is defined as having experienced sexual, physical, and/or emotional abuse, death of a parent, and bullying, or any combination of these factors.

Some important proteins involved in inflammation are called pro-inflammatory cytokines, messenger proteins sent out by immune cells to coordinate with other immune cells and fight off infections and disease. Two relevant pro-inflammatory cytokines are tumor necrosis factor- (TNF-) and interleukin-6 (IL-6). According to Coelho and colleagues' review in 2014, eight studies linked IL-6 and childhood maltreatment. For example, one study (Carpenter et al in 2010) measured adults and found early-life trauma survivors had 13% higher IL-6 levels than controls. TNF- was indicated in 5 studies, with two studies finding it positively correlated with the number

of childhood traumas (Dennison et. al 2012, Tietjen et al, 2012).

It is possible that these cytokines form a direct link from CM to schizophrenia. In one study by Denison and their team, researchers compared people with schizophrenia who had lived through CM and people with schizophrenia without CM histories. The results? Only people with schizophrenia and CM experiences had increased IL-6..

There are many other inflammatory markers that are not cytokines. C-reactive protein (CRP), for example, is released from the liver in response to TNF- and IL-6 levels in the bloodstream. At least eight studies show that average CRP levels of people with a history of CM are increased compared to those without this history. A positive correlation between number of CMs and levels of CRP also exists (Rooks et al, 2012).

The mechanisms for emotional trauma leading to neuro-inflammation is still unknown, but it has been established that neuro-inflammation is associated with psychosis.

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According to an article by Dennison et al in 2012, there is evidence for increased IL-6 release in response to psychological stress. Another study found that people with schizophrenia also tend to have increased IL-6 and TNF- in their bloodstreams compared to those without schizophrenia. Furthermore, Dennison's work shows significant increase in TNF- in those people with schizophrenia who also went through some childhood trauma when compared with people with schizophrenia and no childhood trauma, and a positive correlation between number of CMs and TNF-. A meta-analysis by Miller et al in 2011 chronicled circulating plasma levels of pro-inflammatory cytokines were elevated in people with chronic psychosis and first-episode psychosis. More specifically, Khanaker, Pearson, Zammit, Lewis, and Jones found in their 2014 meta-analysis that IL-6 and CRP are present in people with psychosis. Remember: schizophrenia includes chronic psychosis. So, we can say there is some association between neuro-inflammation markers and psychosis. Recall from the beginning of this article the model that kids who go through CM can grow up to be adults with chronic neuroinflammation. What do we know specifically about inflammation in childhood and increased psychosis risk?

According to Khandaker and colleagues' study in 2014, high levels of baseline IL-6 at age 9 were associated with an increased risk of developing psychosis in young adulthood. The higher the levels of IL-6 were in 9 year olds, the greater the risk for psychotic experiences and the stricter the phenotype for psychotic difforders at age 18. This study also measured CRP levels and found a very similar pattern, though the association was less distinct.

Dennison breaks it down: people who go through early trauma have a greater risk of developing psychotic symptoms, and the more trauma the person goes through, the greater risk they have for developing psychosis, which can also be from severe major depression, bipolar, or schizophrenia later in life.

One well cited meta-analysis by Varese and colleagues concurs. They report findings that childhood maltreatment predicts schizophrenia later in life.

We don't know the mechanism for this risk yet, but considering the existing links between childhood maltreatment and inflammation, and inflammation and psychosis, it is possible that childhood maltreatment is a main factor in neuro-inflammation which is a main factor in schizophrenia, and that childhood maltreatment could lead to psychosis. This link is almost certainly an oversimplification, especially considering the diversity of symptoms that people with schizophrenia have, the variety of CMs possible, and the mysterious mechanisms of neuro-inflammation, but it is worth pondering.

Hold on. If cerebral inflammation is linked to psychosis, would an over-the-counter anti-inflammatory drug work as an adjunct to standard drug treatments? The answer appears to be yes. Several reviews highlight 1000mg/day of aspirin for 3-4 months showing promise, significantly reducing symptom severity of schizophrenia. These results were moderate, and not effective as a replacement of antipsychotic medication. Still, I and many others like me still wade through psychologically-extreme symptoms in school, work, and personal time. I know I'll be speaking to my psychiatrist about adding aspirin to my treatment cocktail when I see her next.

Here's the upshot. The evidence does not conclusively tie development of schizophrenia to neuro-inflammation. Any conclusive evidence would be immensely difficult to obtain, so almost no evidence has been produced. I have presented the evidence for the hypothesis that chronic adult neuro-inflammation as a result of CM can lead to schizophrenia, but there remains evidence against it. There remains ambiguous evidence. There also remains hope for people like me, who could be living happier, healthier lives with progress of new treatment based on reduction of something so common, yet so devastating.