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CURESZ FOUNDATION

Newsletter

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Comprehensive Understanding via Research and Education into SchiZophrenia

The 7 Catastrophic Consequences of Psychotic Recurrences

It is very unfortunate that individuals with schizophrenia relapse repeatedly. The #1 cause for the recurrence of psychosis is either inconsistent adherence to antipsychotic (AP) medications or total non-adherence.[1] The reasons for poor adherence in schizophrenia are related to the illness itself, and patients should not be blamed.

The symptoms of schizophrenia that lead to adherence[2] include:

1. ANOSOGNOSIA
This is the lack of insight that one is very sick with delusions and hallucinations, and so the use of medication is rejected.

2. COGNITIVE DIFFICULTIES
This includes serious memory impairment, which leads to forgetting to take the AP.

3. NEGATIVE SYMPTOMS
These include apathy, lack of motivation and loss of the ability to do many things (avolition), including taking medications every day.

4. SUSPICIOUSNESS
The individual believes that the common side effects of AP medication is evidence of being poisoned.

5. ALCOHOL & DRUG USE
This is very common in persons with schizophrenia living in the community, and being intoxicated or stoned precludes taking prescription medication.

The combination of all those factors inevitably leads to a high rate of nonadherence once discharged from the first hospitalization.

Just like type 1 diabetes or hypertension, where medications must be taken every day or risk relapse, persons with schizophrenia must take

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their oral pills every day without interruption. A published study showed that a drop of only 25% in The AP blood level (which means missing a dose once every 4 days) is enough to cause a relapse in schizophrenia.[3]

Long-acting injectable (LAI) AP were developed in the 1970's, precisely to solve the problem of non-adherence with oral medication. However, due to the lack of scientific advances about the brain-damaging effects of psychosis (which appeared 3 decades later), clinicians back then were completely unaware that psychosis is associated with the dangers of recurring psychosis. They also believed that patients should *"make their own decisions,"* despite the well-known fact that the decision-making region of the brain (frontal lobe) is dysfunctional in schizophrenia. Patients were even led to regard LAI treatment as *"stigmatizing"* and as a *"punishment"* for multiple relapses, so they resisted the LAIs. Now LAIs are regarded as a most compassionate and effective therapeutic approach to save patients with schizophrenia from psychosis-induced brain damage.

Around the year 2000, psychiatric neuroscience research revealed that psychosis destroys brain tissue and causes brain atrophy[4] due to neuroinflammation and free radicals[5] both of which damage gray and white matter. Brain structure and function deteriorate with every psychotic relapse. This prevents persons who develop schizophrenia from ever returning to their baseline preceding the first-episode psychosis (FEP), which is very tragic for young individuals in late adolescence or early 20's.

The following are 7 catastrophic consequences of recurrent psychotic episodes[6] which are due to poor adherence:

1. BRAIN TISSUE LOSS
and brain atrophy and disintegration of the extensive network of myelinated fibers (about 137,000 miles) which connects all brain regions and creates a unity of self.

2. TREATMENT-RESISTANCE
Patients respond to low doses of AP in the first-episode of psychosis (FEP) but need higher and higher dose with each psychotic relapse until eventually they become completely treatment-resistant (and will need Clozapine, which most patients never have access to). The brain structure changes drastically with each episode and that's why AP that previously worked no longer do so.

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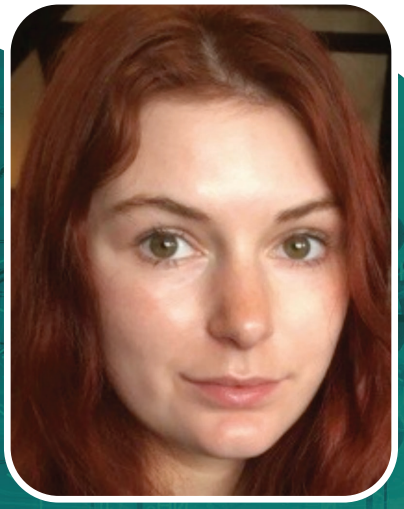
WhatSZ IN THIS EDITION

CureSZ News

SCHIZOPHRENIA SURVIVORS

The Story of Rhea



"I don't have a perfect life, but there are moments where I look around and am so glad that I am alive."

~ Rhea LaFleur

I was born in Potsdam, New York. When I was growing up, I showed warning signs of my illness, but they were dismissed as *"spunk"* or an overactive imagination. I graduated from high school early because I felt out-of-place in the rural, conservative town. I needed a change and chose to attend the University of Southern California, where I received a full-tuition scholarship.

During my second semester, my *"spunk"* and active imagination evolved into a full-blown psychotic disorder. By the time I returned home for the summer, I was convinced I was a computer and that the rest of the world was possessed by aliens trying to eliminate me.

The psychiatric care in my hometown of Potsdam was inadequate and the earliest I could be seen was 3 months. The psychiatrist told my parents that I would need a friend for the long road ahead and recommended a dog. I named the dog Kiwi, and he would become the center of my life.

It didn't take long for me to wind up in the hospital. On the first activity of the first day of my stay, I was told, *"We see kids like you all the time. You will be in here three days and won't ever have to worry about it again."* If only! It was years before that ease of mind was within reach.

I was insistent on returning to USC as if nothing had happened. My mother came to LA with me, supposedly just to get me settled in. She never left, afraid for my safety. I went to an intensive outpatient program every day, had an active extracurricular schedule, and took 18 units of classwork at USC. I have often looked back at that semester and wondered how I managed to juggle all that, but I think I had to. I had to stay as busy as possible, or I would be alone with my thoughts, and my thoughts were scary.

One night I began to babble, unable to construct a sentence. My mother brought me to the hospital, where I was held involuntarily, given the prognosis of *"grave,"* and diagnosed with bipolar-type schizoaffective disorder.

I would stay there for a month, on a 1-to-1 for much of that time as I tried to hurt myself in the hospital. I was watched all day, every day, even when sleeping, using the bathroom, and showering. I took my final USC examinations in the hospital, receiving 4 As and a B+. I briefly stayed in a residential program post-discharge but found it unhelpful.

I took the next semester off, relocating to Boston for programs at McLean. I was hospitalized again and given ECT, which I found unhelpful.

Post-discharge, I began a program at Boston University's Center for Psychiatric Rehabilitation called NITEO. The program aims to aid college students on leave due to mental illness. I went back to USC for an unremarkable semester but returned to Boston afterwards for transcranial magnetic stimulation at McLean. I received this treatment outpatient, so I was able to intern at NITEO, serving as a mentor and confidante for other students and teaching the music and Photovoice classes. I found that even though I wasn't better, I was a master of compartmentalization. I was able to talk to the students, just keeping the attention off me. It was also very helpful that I knew all the adults there and they were very understanding if I simply couldn't be present for a day.

I realized USC was just not going to work, as much as I wanted it to. I transferred to Columbia University and began ketamine infusions. Initially, they were remarkable, reducing my suicidality, but over time the effects began to wane.

I got by for a bit, not thriving in school, and needing constant care from my parents, but managing to stay out of the hospital. Then I began Clozapine, and everything changed. It took a while to get me stabilized on the dosing, but after a few months, life got easier for me. I could suddenly manage my schoolwork, my hallucinations decreased, and most notably, my persistent paranoia waned significantly. No longer was I afraid to go to class, thinking my classmates were poisoning me, or that strangers on the street were plotting to eliminate me. My suicidality also decreased quite a bit. I began to get As, which I hadn't managed to do previously at Columbia. There were downsides as well; side effects like excess saliva production and extreme fatigue, which required more meds. I still had significant depression, which I managed by staying busy, trying to stay out of the apartment, and spending more time with Kiwi. I eventually graduated in May 2020 with a BA in Sociology. I then began a Master's in Disability Studies at the City University of New York, graduating with a 4.0 in May 2022.

I now live alone with Kiwi in a studio I love, do research on OCD and early psychosis at the New York State Psychiatric Institute, and look forward to applying to PhD programs. I try to take Kiwi to the dog park at least twice a day so he and I can both socialize.

CureSZ News

Targeting Brain Energy Metabolism Changes in Schizophrenia

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Association between schizophrenia and altered energy metabolism: Many people are familiar with the fact that some of the antipsychotic drugs used to treat schizophrenia such as olanzapine can cause weight gain, disruptions of glucose regulation, and may predispose to diabetes.[1] However, what is less commonly known is that schizophrenia itself is actually associated with similar changes.[2] In fact, multiple studies have found elevated blood glucose and insulin resistance, hallmarks of prediabetes/diabetes, even in first-episode schizophrenia patients with little to no prior antipsychotic use.[3] While the significance of this association is debated, there is evidence to suggest that these disruptions may actually play an etiological role in schizophrenia and its development.[4]

Importance of energy metabolism to brain function: So, how are energy metabolism disruptions relevant to brain function? Well, it turns out that the brain consumes a lot of energy. In fact, while accounting for only 2% of body weight, the brain consumes about 20% of energy intake.[5] Despite this, it has very little capacity to store energy, and thus is very vulnerable to even minor changes in energy delivery.[5] Most of the energy consumed in the brain goes toward maintaining synapses,[5] the connections between neurons that allow them to communicate. Importantly, dysfunction of synapses is heavily implicated in schizophrenia.[6]

Brain energy metabolism changes in schizophrenia: In schizophrenia, there appears to be a shift in the way the brain utilizes energy with an increased reliance on a process for generating energy from glucose that is much less efficient and generates much less energy overall.[7] Furthermore, this process leads to a buildup of lactate (AKA lactic acid), which causes increased tissue acidity. Indeed, a number of studies have shown evidence of increased acidity in the brains of schizophrenia patients.[7,8] Thus, in addition to less efficient energy production, which directly impacts the brain's ability to maintain synapses, the brain energy metabolism changes associated with schizophrenia further stress the brain through increased acidity.

Schizophrenia brain energy metabolism changes as a potential treatment target: One group looking into this very issue first identified brain energy changes associated with schizophrenia, and then attempted to identify drugs that could reverse these changes. One of the most promising class of drugs they identified includes pioglitazone, which is an FDA-approved medication that increases the body's sensitivity to insulin and is a commonly used treatment for type 2 diabetes.[9] Since as mentioned above insulin resistance is often associated with schizophrenia, use of drugs in this class may be particularly beneficial in people with schizophrenia. This group then treated a mouse model of schizophrenia with pioglitazone and found that it improved memory.[9]

Of note, pioglitazone has also been studied as an add-on treatment to traditional antipsychotic agents in schizophrenia in two clinical trials though they were both relatively small studies.[10,11] In addition to improvements in measures of energy metabolism (e.g. decreased glucose, improved insulin sensitivity, and improved lipid profiles), schizophrenia patients receiving pioglitazone also had improvements in depressive and negative symptom scores.[10,11] While there is often a focus on treating the positive symptoms of schizophrenia, which include delusions and hallucinations, the depressive and negative symptoms of schizophrenia, which include things like social withdrawal, decreased motivation, decreased speech, and diminished ability to experience pleasure, are often the most debilitating symptoms and the least responsive to traditional antipsychotic medications.[12] Thus, improvement in these symptoms is a really important finding.

Future Directions: While the clinical studies of pioglitazone are promising, as mentioned above, they are relatively small and need to be replicated in larger study samples. Still, they offer a glimpse and demonstrate the importance of targeting brain energy metabolism changes in the treatment of schizophrenia. For one, it may prove an effective way of improving negative and depressive symptoms of schizophrenia. Furthermore, it may also improve broad metabolic changes such as elevated glucose and decreased insulin sensitivity associated not only with schizophrenia but also many of the antipsychotic agents that are the current mainstays of treatment. This is incredibly important as these metabolic changes likely contribute to the greatly increased rate of premature death seen in individuals with schizophrenia.[13] Thus, continued studies targeting the reversal of metabolic changes in schizophrenia have great potential for not only improving the treatment of this illness but also for reducing its associated early mortality.

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The 7 Catastrophic Consequences of Psychotic Recurrences *(continued from page 1)*

3. FUNCTIONAL DISABILITY
and inability to return to school or college or to work, whatever patients were doing before the FEP. Thus, with repeated relapses, those young people become totally disabled instead of being productive members of society.

4. INCARCERATION
A high proportion of patients with schizophrenia are arrested and jailed when they become psychotic and behave erratically. Then they are sentenced to prison. They no longer get admitted to state hospitals (because they have all been shuttered), and so are surrounded by armed guards instead of doctors, nurses and social workers who compassionately provide them with medical care instead of being thrown into a prison with murderers and rapists.

5. SUICIDE
Many people are not aware with the incredibly high rate of suicide among young people with schizophrenia when they relapse. Some studies report over 10,000% higher[7] death rates from suicide compared to young persons of the same age in the general population.

6. HOMELESSNESS
Drug abuse, chaotic life-style and living on the side-walks of large cities, with risk of becoming victims of crime.

7. STIGMA
Psychosis can cause unusual behavior, poor dress and grooming, and intensify the public's negative bias against serious mental illness.

Yet against this dismal outcome, there is hope and good news for persons with schizophrenia. The use of LAI very early, i.e. immediately after the first hospitalization, can make a huge difference in preventing deterioration. There are published studies that relapses in the first year after the FEP if LAIs are started is 650% lower than the rate of relapses in patients receiving oral AP.[8] I have personally had patients who did not relapse for 5 continuous years after switching them to injectable AP. Preventing relapses is vital because recent research demonstrates that disability actually begins after the second, not the first episode of psychosis.[9] Thus, preventing the second episode is the key to remission and recovery in schizophrenia. Thus, the deterioration and downhill course of schizophrenia can be prevented in most patients by using LAI AP right after the first hospitalization for schizophrenia.[10]

There are other important advantages to using second-generation LAI formulations. 24 published studies report that they are neuroprotective (i.e. help preserve the brain tissue integrity).[11]

Also, a 7-year follow-up study in Sweden reported that a second-generation LAI antipsychotic was associated with the lowest mortality rate from all causes.[12] This is very important given the high premature mortality in schizophrenia.

In summary, until a cure for schizophrenia is discovered, the best way to give patients a chance to return to their baseline and avoid the tragic, life-altering consequences, is to use second-generation LAIs immediately after discharge from the first hospitalization. Yet, inexplicably, this is rarely done, and 99% of clinicians in the country prescribe pills and do not use LAI AP for several years until patients have already relapsed several times. By that time, the patients have already lost substantial amount of brain tissue and have become disabled and have been criminalized and incarcerated. Imagine how much different the landscape of schizophrenia would be if clinicians prevented any further episode of psychosis after the first one. Many young people with a diagnosis of schizophrenia may be able to return to their baseline, further their education, get a job, get married, raise a family and exercise their constitutional right to pursue happiness.[13]

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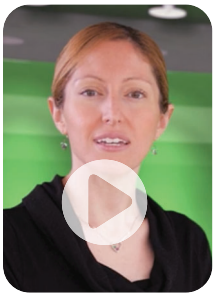

VIDEO HIGHLIGHT

How to Connect with a Schizophrenia Caregiver

by Catherine Engle, LPCC-S

Click on photo to view video.

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Your contribution will help provide education and referrals to persons with schizophrenia, their families, and those who work with the seriously mentally ill. CURESZ informs the general public to better understand this serious brain disorder, and to provide scientific advances showing that there is hope for recovery, and a return to a fulfilling and normal life. The CURESZ Foundation is a 501(c)(3) nonprofit organization. All contributions are tax deductible.

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