
A Hypothesis: Schizophrenia is a Neurological Disease

BY Michael I. Rose, MD, FAPA

Psychiatrists are sometimes heard to say that schizophrenic patients have “their wires crossed.” To wit, loose associations consist of statements that reflect intrusive thoughts appearing out of context to an initial line of thinking. Nevertheless, when traced, each intrusion has its origin within the thoughts of the patient although the connections are not always clear.

When properly traced, each thought separately makes valid sense to the individual. It seems as if the thinking process is running on one track and switches to another track. Is this the process that actually occurs?

**The neurological pathophysiological answer is unknown at this time.
Hopefully, one day it will all be clear.**

It appears as if, when these “switched-track thoughts” occur in volume, the patient complains of confusion and the observer sees a primary thought order — the essence of this disease.

When a sufferer relates a little story which is out of reality, we often see simple origins within the person’s life.

An intense belief that the sufferer is the Archangel Joshua fighting in outer space against unseen enemies reflects a simple connection between a sufferer’s wish to aid their friend Joshua who is beset with difficulties that the sufferer has promised to fix. The underlying affection for Joshua, the compassion for this friend, and hope for him are clear, but unstated and unaware to the sufferer.

A deep understanding by a trained observer makes the story easy to understand. Those outside the circle might see that only as a delusion; if visual or auditory, as an hallucination.

In a different context; if the “wires get crossed” and the formerly completely peaceful schizophrenic designates a concrete human being as a dangerous enemy resulting in murder, we call the perpetrator a criminal.

Legal distinctions ask the patient if he knows right from wrong, demonstrating a tragic misunderstanding of the disease. All analogies are imperfect. However, one is that of two electrical wires losing their insulating cover thus causing a short circuit and perhaps a fire. If you look at other areas of the wired circuits you could not see the short. The wires act as they do because they are crossed and short out (a disorder of synchrony?) — not because of right and wrong. It is a simple immutable law of physics.

A Turkish fable tells of an individual who passes by a man tossing pebbles into a lake. He asks the man why he is doing that and the tosser says “I’m trying to turn the lake into yogurt.” The passerby says “That’s impossible,” to which the tosser replies, “Yes, but imagine if it were possible and the lake was yogurt!”

Asking perpetrator schizophrenics if they understand right from wrong is like tossing pebbles into the lake. The idea may seem attractive but it is the wrong process — it is out of reality. This phenomenon of “wires crossing” may be temporary (“leakage” = a disorder of synchrony) from one axon to another. The axons are ensheathed in myelin.

But why would there be leakage, a disorder of synchrony?

If we suggest that the proper construction of myelin depends on the strength of various feelings, several speculations arise to an unknown answer.

We know that myelin is laid down both in greater volume and better quality when individuals pursue ardent interests such as music, sports, etc. Genetic factors, varying with each individual, regulate these constructions. Diffusion tensor imaging (DTI), a type of magnetic resonance technology can show white matter in action.¹ “The functioning of white matter may be just as critical to how people master mental and social skills.”¹ “Many people who suffer bipolar disorders or schizophrenia have a defect in the gene that regulates production” (of the protein neuregulin that coats axons).¹

On the contrary, what factors result in inefficient myelin formation resulting in later collapse? Are these environmental or genetic factors or the interplay of both? Is it related to lack of parental compassion for the child’s feelings, to wanton destruction of the child’s quest for mastery? Does poor training in how to handle conflicts cause excess anxiety at some time in the future resulting in failure of the wrappings of the axons of the nerves that carry our thoughts? “Children who suffer severe neglect have up to 17% less white matter in the corpus callosum.”¹

“Brain volume decrement was due to shrinkage of the neuropil surrounding the neurons in the gray matter, including reduction in dendrite length by a half and a decrease in the number and size of dendritic extensions.”²

“The vulnerability of the myelination process likely contributes to the unique susceptibility of the human brain to highly prevalent disorders of development. A dysregulation in this developmental process is hypothesized to result in an insufficient capacity to maintain temporal synchrony of the brain’s widely distributed functional neural networks and manifests in the heterogeneity of symptoms and cognitive impairments that characterize disorders such as schizophrenia.”⁸

Much research has been made regarding the effects of drug treatment. “Neurotransmitter actions trigger various neuroplasticity cascades to rebuild the neural pathways ravaged by recurrent episodes of psychosis or depression.”²

“The risperidone-treated subjects demonstrated changes in grey matter and white matter in several brain regions including superior temporal gyrus.”⁹

It has been suggested that the ability of individuals to cope with and resolve stress has a genetic basis. Genes determine neurological structure. Does their influence often vary with various environmental interactions, including psychological experiences? Schizophrenia has been thought to evolve when an individual would seek another reality to live in when they cannot cope with the anxiety of dealing with the real world. Is it possible that first, there is a genetically determined neurological deficit in coping with conflict and later, when intense unresolvable anxiety mounts, further neurological damage occurs causing schizophrenia?

Clinically, many specialists have seen the following: You call a 40-year-old schizophrenic who was recently discharged from the hospital at his parents’ home and ask to speak to the patient. A parent answers, complains that you ask too many questions, says their child is not there, won’t hand the phone to your patient, etc., and hangs up. How was that child treated when the child was four years or four months?

Other diseases may be related to these issues.

Clinically, many specialists have seen the following: You meet the parents of an autistic child at their home. They are carrying the one-year-old child as if they are carrying a burning log. They snuggle the infant's head while looking away from the child.

Nevertheless, autism is a neurological disease caused by genetic factors.

Other diseases are caused by failure of the myelin sheaths, the axon wrappings. Multiple sclerosis is one; neurologists know of many others.

“Autoimmune-mediated demyelination and axonal degradation of the central nervous system neurons are critical processes in Multiple Sclerosis.”⁴

“Dyslexia results from disrupted timing of information transmission in circuits required for reading,” and “brain imaging has revealed reduced white matter in these tracts.”¹ “We’d love to find a way in which we can address white matter problems early on in childhood in a way that would help the white matter to mature and the white matter connections to develop most efficiently.”³

“White matter abnormalities in cortico-striato-limbic networks confer vulnerability which increases the likelihood of chronic geriatric depression.”⁵

“Microanatomical abnormalities might predispose certain elderly people to be resistant to antidepressant therapy.”⁵

“Peripheral neuropathies may be due to nutritional deficiencies causing axonal loss and/or demyelination which, when measured by nerve conduction studies, may show slowing of velocity and/or loss of amplitude.”⁶

“Wilson’s disease is related to an abnormality of copper metabolism. Symptoms include tremors, dystonia, dementia and psychiatric disturbances of all sorts, including affective disorders, psychoses, personality changes and behavioral abnormalities.”⁷

This Hypothesis pursues increased understanding. Is it all genetic?

What causes the neurological process of inefficient myelin, myelin breakdown and “leakage” (a disorder of synchrony)? Why one person and not another? Hopefully, further research may lead to better treatment or even prevention allowing many individuals to have happier lives.

Perhaps the psychological factors are totally unrelated. Or perhaps the environmental psychological experiences determine how the genes regulate the neurological processes.

How many individuals have had similar childhood experiences yet never suffer from schizophrenia or autism? Patients have their childhood studied in great detail by specialist scientists. Yet how many non-patients are studied to that extent?

“Schizophrenia is now understood to be a developmental disorder that involves abnormal connectivity. White matter is abnormal (possessing fewer oligodendrocytes than it should) in several regions in the schizophrenic brain. Many of the mutated genes linked to schizophrenia caused by aberrant genes were involved in myelin formation.”^{1,10}

Could it be that other psychotic diseases such as bipolar disorder have similar origins?

Is it useful to differentiate two different disciplines within the same organ — neurology and psychiatry? In some ways, yes, in others, no.

Most of these conundrums end up as two disciplines complimenting each other — neuropsychiatry.

Further study is required.

I consider it a privilege to make this contribution.

Postscript

When I read in Scientific American that schizophrenia was a “developmental disorder that involves abnormal connectivity ... white matter is abnormal,” I felt as if I had been hit with a ton of bricks. This explained many of the unanswered questions that have drifted along for many years.

I dashed to my computer and watched as my fingers danced on the keyboard as a tsunami of stream of excited consciousness flowed until exhaustion took over.

Schizophrenia is a neurological disease! Emotions affect all bodily processes in many ways including inhibition or stimulation.

Several days later, I had an awakening, best described in an email I sent to some London friends, a very gentlemanly British solicitor and his lovely wife. (I had previously sent the paper “Schizophrenia is a Neurological Disease” to these friends.)

Several days after writing the paper I was awakened at 4:32 am with the notion that if we consider schizophrenia as a neurological disease, how would that affect the parents who feel guilty about having caused it?

Also, payment for psychiatric illness in America is not in parity with other illnesses. However, as a neurological disease one might think it would be correct to modify that here, in the "Greatest Country in the World."

Again, if a schizophrenic commits a crime, they are warehoused, costing \$40,000 per year, in prisons and abused rather than placed in a secure half-way house where patients are given jobs, medication and are self-supporting. As a neurological disease there may be more interest in a therapeutic environment.

Regarding the forensic arena pertaining to other neurological diseases, if an automobile driver has a first-episode epileptic seizure causing trauma to another person, the driver is not put in jail.

You live in England where they consider America the “Land of the Savages.” It’s something to think about. While studying medicine in Lausanne, I spent two summers as a medical extern in Sheffield with their medical students. I was always fascinated as how civilized the Brits were (I was raised in the jungles of Brooklyn, New York where one never heard the words "Thank You" or "Please").

In Sheffield, on internal medicine rounds, the attending physician would discuss the case something like this: This is Mrs. A whose husband is disabled; they have three children so she brings in neighbors’ laundry to earn a few quid. This is particularly difficult for her as she has ulcerative colitis which, as you know, often is associated with arthritis, making her job excruciatingly painful. Our first responsibility is to rid her of the colitis and then the arthritis.

When I came to America, the rounds went something like this: The attending physician would stand at the door of a room where a dozen clinic patients were and say; there’s the brain tumor, that’s the breast cancer, that one has colitis, that lady is afraid she has breast cancer so we are going to remove them tomorrow, there’s the loony with a heart attack who came to the emergency room several times, no one examined him

thinking he was imagining it until one of the nurses did an electrocardiogram and diagnosed it, etc.

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