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Unraveling the Mystery of Autoimmune Encephalitis: Navigating Life and the Science of a Rare Disease

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Unraveling the Mystery of Autoimmune Encephalitis

Navigating Life and the Science of a Rare Disease

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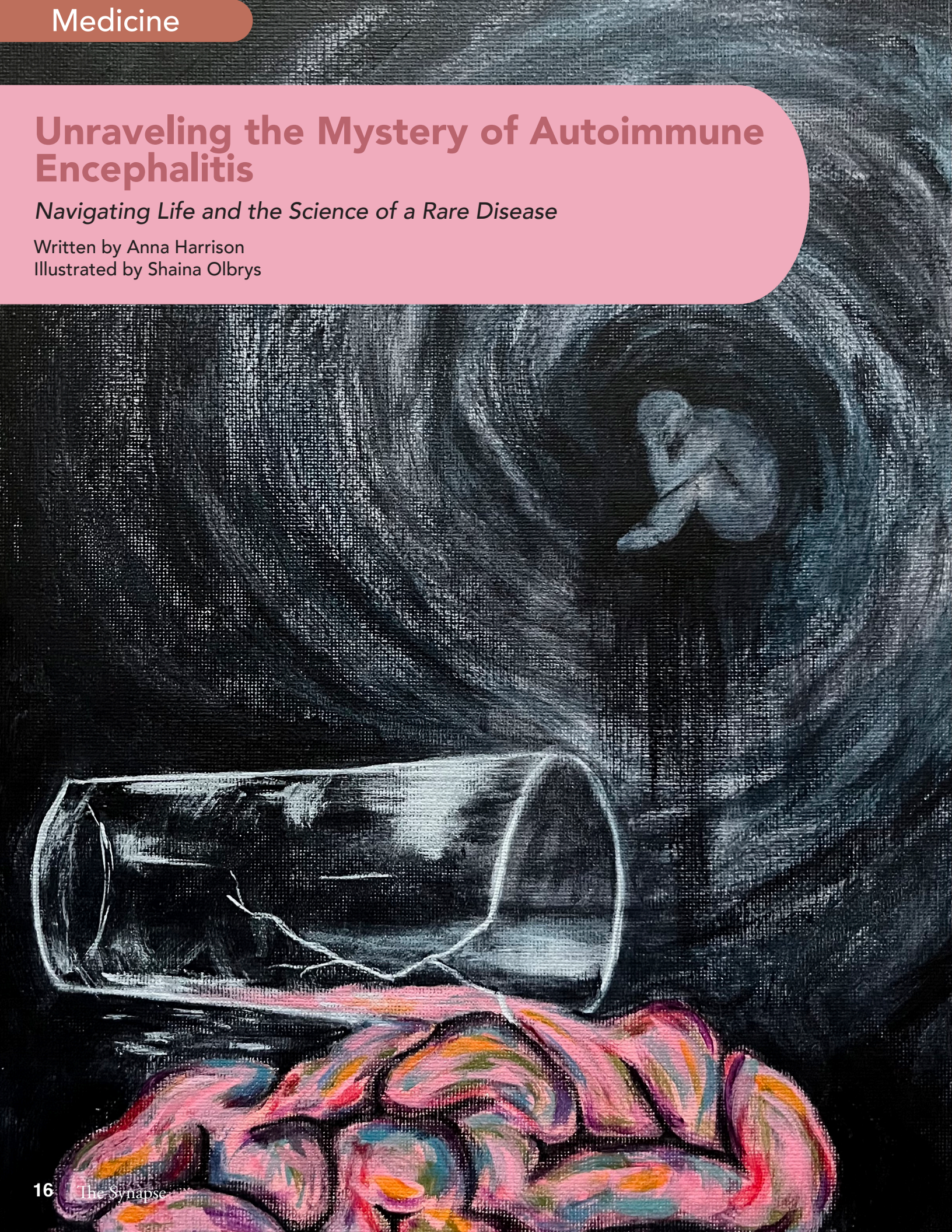

A rare and frequently misdiagnosed disorder, autoimmune encephalitis is, to most, a meaningless jumble of scientific jargon. To the medical community, autoimmune encephalitis is an elusive central nervous system disease characterized by antibody-mediated destruction of various parts of the central nervous system. Besides some immunomodulatory therapy, the patients with the misfortune of falling ill with this disease are at its mercy. Autoimmune encephalitis was my teenage experience.

Just barely getting used to being tall enough to reach the sink, I stand over it with a blank stare and my plate of half-eaten toast. I know what I am here to do because I have done it every day for every meal since I can remember. I am here to clean my plate and wash my dish — a task so automatic, yet here I stand, utterly paralyzed. I am searching my brain, but the wires just are not firing. Or connecting. Or they are, and they are screaming as loud as they can to tell me what to do, but no matter how hard I try, I just cannot understand them.

I cannot remember how to turn on the sink.

Just as I eventually remember that I need to reach up my hand, grab the faucet handle, and turn it so the water will flow out, a panic sets in. The silence around me is deafening, and I am suddenly horrifyingly aware that I am home alone. I do not know why this horrifies me, but it does. I do not know where any of my family is, how long they have been gone, or if they are coming back. I reach for the landline to call my mom. My heart pounds harder with every ring. Do you not remember, Anna? I just told you I was leaving for the grocery store 5 minutes ago…

I did not remember.

A complete loss of self is the best way I can describe this disease. The root cause is not yet known. It is difficult to diagnose clinically, and treatment options are effective but harbor grim and long-lasting side effects. The relapse rate is significant. It could come back at any time and usually does. It did for me a decade later.

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Autoimmune encephalitis, once considered rare and confined to a small group of people, has recently been diagnosed at increasing rates. Its clinical etiology has expanded significantly, and it is now characterized as the most common cause of encephalitis. Memory loss was one of many of my symptoms, but the disease can present itself in clinically diverse ways. The molecular underpinnings of the autoimmune encephalitis phenotypes have been probed over the last two decades, and spearheaded by research under Sarosh R. Irani, B.M.B., Ch., D.Phil., at the University of Oxford and Mayo Clinic. A number of pathogenic autoantibodies (involved in inflammation and tissue injury) directed against discrete neuroglial antigens have been identified, each with their own unique clinical profile of disease. Understanding the pathophysiology of the autoantibodies at the root of the disease is of great clinical importance. Patients like myself, who were once limited to one or two poor treatment options and few answers regarding the true nature of their disease, now increasingly have access to detailed, highly sensitive disease detection and characterization methods that can significantly expand treatment options and improve patient outcomes.

Central to these discoveries have been methods probing the immunobiology of patient samples and the development of robust diagnostic assays that maintain the native state of neuronal surface proteins. Historically, this has involved the incubation of patient sera (a protein rich liquid derived from coagulated blood) with live neuroglial cells, followed by immunohistochemistry to identify patient antibody-neuron binding. This is thought to facilitate a violent autoimmune attack against the neuron or disrupt neuronal function in some other way — for example, by inhibiting

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the functionality of an ion channel. Based on the localization of binding and measured electrophysiological consequences of binding, specific neuronal proteins can be probed for patient autoreactivity via selective expression on non-neuronal human cell lines. This is supported within the context of patient symptoms and prior field research.

Once the target antigen is identified, in vivo (in a living organism), in vitro (in a test tube), and ex vivo (outside of the living organism) methodologies are employed to understand the molecular features of the antibody. This includes looking at the epitope, where antibodies attach to antigens, and affinity/pathogenicity maturation – a process where B cells increase their affinity/attraction to a specific antigen. Each of these cutting-edge techniques helps researchers understand what specific molecular feature is causing differing symptomatology and ultimately works toward developing more effective therapeutics with fewer side effects.

The future of this research will focus on understanding this pathogenic evolution and the cause of these diseases – which remains a clinical mystery. To help achieve this researchers are investigating newer techniques, such as single-cell RNA sequencing to understand the pathology and clonal expansion of cells that secrete these pathogenic antibodies in and out of the central nervous system. Autoimmune encephalitis research has come a long way since the monumental discoveries of discrete antigens. However, a significant amount of work remains to be done until patients like me can face a better path. Robust clinical testing is still not widely available, and many doctors are ill-equipped with outdated concepts of this disease.

As we forge ahead, the increased awareness of autoimmune encephalitis, the empowerment of patients, and the pace of discovery in the field give hope to all of us whom this disease has touched Hope that a brighter future awaits — one marked by improved understanding, timely interventions, and enhanced quality of life for those navigating the complexities of autoimmune encephalitis. • • •