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Neuronal Hyperexcitability: The Elusive Link Between Social Dysfunction and Biological Dysfunction

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Abstract: Human society is a macrocosm of the human body. Hence, it should not be surprising that a physiological abnormality that can disrupt virtually every system of the human body can disrupt virtually aspect of human society. According to the multi-circuit neuronal hyperexcitability (MCNH) hypothesis of psychiatric disorders, an inherent hyperexcitability of the neurological system drives the wide range of psychological, emotional, and behavioral disturbances that together are referred to as "mental illness." It also drives the plethora of autonomic, endocrinologic, metabolic, and immunologic disturbances that have been linked to mental illness. The means by which the neuronal hyperexcitability trait has these diverse effects is that a pathological elevation in neural signaling causes chaotic electrical signals to be sent both to the mind and to the various organs and systems of the body. The chaotic signaling to the mind causes the mental, emotional, and behavioral problems, and the chaotic signaling to the body causes the chronic medical problems with which the trait is associated. But beyond these effects, the neuronal hyperexcitability trait drives nearly every major social problem in society, including domestic violence, child abuse, abortion, substance misuse, unemployment, homelessness, and criminality. The means by which the trait drives all of these social problems is the same as that by which it drives all of the aforementioned psychiatric and medical problems because human society is made of billions of human beings, and nearly half of the world's population harbors the trait of neuronal hyperexcitability. This article will take a detailed look at how the common but elusive trait of neuronal hyperexcitability translates into all of the psychiatric, medical, and social problems that have been plaguing humanity since antiquity and offer a practical intervention that has the potential to change the world.

Keywords: Neuronal Hyperexcitability, Pathophysiology of Mental Illness, Mind-Body Connection, Biomarkers of Disease, Preventive Medicine, Anticonvulsants, Mood Stabilizers, Neuroregulators

1. Introduction

Modern society is rapidly unraveling. Parents are fighting with one another, kids are bullying one another, substance abuse is rampant, suicide rates are soaring, criminality is at an all-time high, jails are over-crowded, and healthcare costs are spinning out of control. In addition to the tremendous emotional, physical, and financial toll that all of these problems are taking on society, the erosion of trust that they are causing is rapidly leading to gridlock in the world's social, political, and economic systems. Though numerous efforts have been made to control these problems at a systems level, most have met with limited success. That underscores the need to better understand what factor or set of factors might be driving the rapid deterioration of society that is being witnessed today. If there were some core abnormality in the people who make up society, and that abnormality could be detected and therapeutically modified, it could, over time, effect significant change. This article will identify such an abnormality and discuss the simple way that it can be detected and therapeutically modified so as to change the trajectory of the biological, psychological, and social problems that the world is facing today.

Most behavioral abnormalities are caused by mental illness, and although the underlying cause of mental illness remains unclear, converging lines of evidence suggest that mental illness is rooted in an inherent hyperexcitability of the neurological system [1]. According to the multi-circuit neuronal hyperexcitability (MCNH) hypothesis of psychiatric

disorders, an inherent hyperexcitability of the neurological system drives the wide range of psychological, emotional, and behavioral disturbances that together are referred to as "mental illness" [1]. It also drives the plethora of autonomic, endocrinologic, metabolic, and immunologic disturbances that have been linked to mental illness [2]. But beyond these effects, neuronal hyperexcitability is thought to drive nearly every social, economic, and legal problem in society, including domestic violence, child abuse, abortion, substance misuse, unemployment, homelessness, and criminality. What makes this discovery so important is that an estimated 40% of the world's population is thought to harbor the trait of neuronal hyperexcitability [3].

The means by which the neuronal hyperexcitability trait causes all of the aforementioned psychiatric and social problems is that hyperexcitable neurons cause the mind to race and emotions to surge in response to day-to-day stressors. According to the mind-brain hypothesis of the cognitive-emotional system [4], mental and emotional stress cause the mind, like stones being thrown at a beehive, to overstimulate the associated neurons and circuits in the brain. The resulting increase in neurological activity causes the same thoughts and emotions to be re-experienced, thus leading to a vicious circle of mutual overstimulation between the mind and the brain. Normally, this process is modulated by neurological self-regulatory mechanisms. However, those mechanisms are partially compromised in carriers of the neuronal hyperexcitability trait [1], thus increasing their propensity to overreact to stress. Their overreactions to stress are expressed psychiatrically by such phenomena as defensiveness, hostility, impulsivity, substance misuse, clinical depression, social withdrawal, suicidality, homicidality, and criminality.

The means by which the neuronal hyperexcitability trait causes the previously mentioned biological disturbances is the same as that by which it causes the aforementioned psychiatric and social disturbances. Pathologically hyperactive neural circuits overstimulate the autonomic nervous system, the endocrinologic system, the metabolic system, the immunologic system, and other systems of the body. Over time, this pathological overstimulation increases the risk of a wide range of chronic medical conditions, including diabetes, high blood pressure, cardiovascular disease, autoimmune disease, cancer, and dementia [2].

Unfortunately, however, carriers of the neuronal hyperexcitability trait are usually unaware that they harbor the trait. Hence, they assume that their stereotypical ways of thinking and behaving are unalterable parts of their personality and that the chronic medical conditions that they develop are an inevitable part of aging. Also, being largely stress-dependent, the effects of the neuronal hyperexcitability trait generally remain dormant until an affected person's stress levels begin to rise appreciably. This gives carriers of the trait the false impression that their responses to the stressors in their lives are due solely to the stressors themselves. Moreover, if anyone attempts to comment on their hyper-reactivity, they tend to become defensive, not willing to admit that they might have a problem handling stress.

Yet, for many reasons, these misperceptions are understandable. First, it is not intuitively obvious that the brain is a different entity than the mind [4]. Hence, when thoughts, emotions, and behaviors are being disrupted by the hyperactive brain, it is only natural to misattribute that influence to the willful intentions of the individual. Second, educational resources about the neuronal hyperexcitability trait are virtually non-existent because the problem is still largely unrecognized, even among healthcare professionals. Third, anything in the area of emotional and behavioral health incurs the stigma of mental illness, which continues to discourage affected persons from seeking treatment. These barriers to understanding underscore the importance of initiating a massive campaign to educate both the medical community and the public about the ubiquitous problem of neuronal hyperexcitability. Until then, the multitude of psychological, emotional, behavioral, medical, social, occupational, and legal problems that are being fueled by the neuronal hyperexcitability trait will not just continue to flourish but will continue to escalate because the stress that they create will continue to add fuel to the fire in the hyperexcitable brain.

2. How the Significance of the Neuronal Hyperexcitability Trait Has Managed to Remain So Elusive

The principle barrier to recognizing the significance of the neuronal hyperexcitability trait has been the lack of clarity about the distinction between the mind and the brain. The prevailing view is that thoughts and emotions are purely manifestations of complex brain function. It is thought that because neural signaling induces magnetic fields, those magnetic fields are the only source of human thoughts and emotions [5, 6]. However, this reductionist view would reduce human beings to mindless automatons whose thoughts, feelings, and actions were dictated by the whims of biological processes and neurological reflexes. Such a simplistic view would also fail to explain where the will comes from, where the attentional element comes from, and, in a broader sense, who the person is that is experiencing the effects of the neurological activity.

Still, some would argue that the brain, together with the rest of the body, is the person. However, neither the brain nor the body have perceptual ability. This is clearly demonstrated by the clinical effects of a severe spinal cord injury. For example, in a "complete" injury of the spinal cord at the level of the neck, none of the neurological activity that would be activated by sensory receptors in the person's arms, legs, or anywhere else in the body below the point of injury would be perceived. The neurological system would be active, but the person would not be able to perceive it. If, however, the ascending neurological input were to somehow traverse the point of injury in the neck and reach the head, the person would be able to perceive it. This implies that the perceptual

element must be somewhere in the head. However, the perceptual element could not be part of the brain because the brain, both structurally and functionally, is part of the neurological system, and as illustrated by the example, the activity of the neurological system cannot be perceived without the perceptual element. The only logical conclusion is that perception must be a function of the mind, which is in the head of the person [4].

Additionally, it is self-evident that the mind has the ability to exert effort. It takes mental effort to concentrate; it takes mental effort to push one's self physically; it takes mental effort to tolerate pain; and it takes mental effort to grapple with intrapsychic conflict. Effort involves energy, and energy induces magnetic fields. At the same time, neurological processes induce magnetic fields as neurons depolarize and repolarize. Hence, the mind and the brain are naturally poised to communicate in the same language; namely, electromagnetic energy. In accordance with Faraday's Law [7], mentally-induced magnetic fields could stimulate the production of action potentials [8], and action potentials could induce the production of magnetic fields [6].

That a two-way dialogue between the mind and the brain actually occurs has now been demonstrated experimentally. Recording from single neurons in patients implanted with intracranial electrodes for clinical reasons, Cerf et al. [9] found that willful thoughts and intentions readily stimulated specific neurons when subjects were asked to perform specific mental tasks. Conversely, Penfield [10], in his seminal work on brain mapping, had found that stimulating different parts of the human brain with an electrical probe triggered different thoughts and emotions. Importantly, this bidirectional influence between the mind and the brain could help explain why psychiatric symptoms tend to develop under the influence of mental and emotional stress. The mind, when under stress, could overstimulate specific neurons and circuits, thus causing them to become hyperactive. The hyperactive neurons and circuits could, in turn, reactivate the associated thoughts and emotions. This would result in a vicious circle of mutual overstimulation between the mind and the brain that could, over time, cause the associated thoughts and emotions to become abnormally intense and abnormally persistent.

Nonetheless, the idea that the mind is a distinctly different entity than the brain has largely been repudiated by most neuroscientists, who have instead sought to understand psychopathology by studying the brain alone. However, to do so is like trying to understand how an automobile turns on and off and drives from point A to point B without recognizing that the vehicle is being driven by its owner. The failure to recognize the mind as a separate entity than the brain also prevents one from appreciating the significance of neuronal hyperexcitability because apart from the agitating effect of mental and emotional stress, the neuronal hyperexcitability hypothesis would fall short of offering a logical explanation for the development of psychiatric symptoms. However, once the independent function of the mind is recognized, it becomes easy to see how a hyperexcitability of the neurological system could increase one's vulnerability to developing psychiatric symptomatology.

3. What Causes the Neurological System to Be Hyperexcitable

Strikingly, the top candidate genes for the major psychiatric disorders — disorders that together express all of the most common psychiatric symptoms—involve ionchannelopathies [11-14]. Specifically, the protein products of the candidate genes fail to adequately regulate the firing of neurons, thus increasing the excitability of the neurological system. Based on extensive clinical observations, the candidate genes appear to be passed down in an autosomal dominant distribution [1]. Recognizing the genetic nature of the neuronal hyperexcitability trait is, for several reasons, critically important. First, it could reduce the feelings of shame that affected persons might feel if they thought their difficulty handling stress was due to mental weakness. Second, it could help affected persons understand that their vulnerability to stress is lifelong and, thus, could necessitate life-long treatment. Third, it could help reduce the stigma that has been perpetuated by the psychologically-based idea that psychotropic medication is a crutch for the mentally weak. Stigma could also be reduced by the user-friendly, fittingly-descriptive acronym that describes what is being treated in persons with neuronal hyperexcitability. In recognition of its genetic origin and its effects on both the limbic and autonomic nervous systems, the clinical manifestations of the neuronal hyperexcitability trait could aptly be described as familial limbic autonomic system hyperexcitability or "FLASH" [2]. Moreover, because the neuronal hyperexcitability trait is also thought to underlie a wide range of general medical conditions, the use of the term "FLASH syndrome" would not necessarily specify the presence of psychiatric symptomatology. This would help prevent it from becoming stigmatized while at the same time broadening its applicability to the wide range of other chronic health conditions that it is thought to underlie [2].

4. Determining the Trajectory of FLASH Syndrome

There are six factors that combine to determine the trajectory of FLASH syndrome. These are: 1) the level of neuronal excitability; 2) the degree of environmental stress; 3) the age at which the environmental stress first begins; 4) the modeling behavior of the parents and other caregivers; 5) the degree of connectedness of the neurological system; and 6) the willful choices of the individual.

4.1. The Level of Neuronal Excitability

As previously mentioned, a study of the families that are affected by the neuronal hyperexcitability trait suggests that the candidate genes are transmitted in an autosomal dominant

distribution. That a classic Mendelian distribution can be recognized suggests that most of the candidate genes that have been linked to mental illness make small contributions in comparison to a few genes that make large contributions and may by themselves be enough to markedly increase one's vulnerability to developing some form of psychopathology. The genes for neuronal hyperexcitability also appear to be additive and severity-specific. That is to say, some of the variants translate into greater cognitive-emotional dysfunction than others, and if one gene variant is inherited from each parent, the severity of symptoms is likely to be greater than if only one gene variant is inherited [3]. This would be due to the lack of an allele that could partially compensate for the failure of the abnormal allele to adequately regulate the firing or neurons. From a clinical standpoint, the more hyperexcitable the neurons are, the greater the likelihood that they will cause some form of psychopathology and the more severe that psychopathology is likely to be. This follows from the idea that hyperexcitable neurons tend to amplify and perpetuate normal thoughts and emotions, an effect that is precisely what distinguishes psychiatric symptoms from normal thoughts and emotions.

4.2. The Degree of Environmental Stress

Because neuronal hyperexcitability is kindled by stress, the symptoms would depend upon the severity and duration of the stress. The higher the stress levels and the longer they persisted, the more hyperactive the affected circuits would become, and the more severe the symptoms would tend to be.

4.3. The Age at Which the Environment Stress First Begins

The younger an affected person is at the time that his or her stress levels begin to rise appreciably the greater the risk that the associated cognitive and emotional distress will drive the development of secondary psychological problems. That's because the young mind has not yet had the opportunity to develop healthy object relations and mature coping mechanisms. This is the MCNH explanation for the tight link between severe childhood stress and the development of personality disorders. Conversely, if the first experience of high stress-levels were delayed until an affected child were more mature, the prognosis would be much better because a mature mind tends not to develop as much intrapsychic tension as an immature mind and, thus, would not perturb the brain as much as an immature mind. The development of mature coping skills helps explain why some persons seem to "grow out" of mental illness. Conversely, persons with poor coping skills tend to become more symptomatic as they age, particularly if their neurons are very hyperexcitable and their levels of environmental stress remain very high [15].

4.4. Modeling Behavior of the Parents and Other Caregivers

Children tend to internalize the attitudes, values, and coping strategies of their caregivers. Also, many of these influences occur at a preverbal age. Consequently, children who are raised in dysfunctional households can be psychologically scarred for life. Moreover, the risk of this occurring is increased when the neurological system is constitutionally hyperexcitable because neuronal hyperexcitability amplifies stress. Unfortunately, these two factors—dysfunctional family dynamics and genetic predisposition—tend to co-occur because parents who have high levels of neuronal excitability tend to bear children who have high levels of neuronal excitability.

4.5. The Degree of Connectedness of the Neurological System

Based on the premise that the locus of hyperactivity migrates around the hyperexcitable brain via the electrical and chemical connections between neurons, the more of these connections there are, the more active the brain will tend to be and the greater the likelihood that symptoms will oscillate back and forth and meld into one another. Clinically, this would manifest as symptom-instability, a phenomenon that would make it more difficult for the affected person to achieve consistency in his or her habits, lifestyle, and relationships. Based on advanced counting techniques, the human brain has an estimated 81.6 billion (+/- 8.1 billion) neurons [16], and with each neuron forming connections with up to 15,000 other neurons [17], there is plenty of room for variance in the number of neuron-to-neuron connections the brain can have. Hypothetically, each extra connection would increase the risk of aberrant circuit induction, as would the degree of neuronal excitability. Although both of these factors can change over time, individual differences are usually the most prominent, thus explaining why the frequency with which symptoms cycle can vary between patients and can even vary within the same patient, although each patient tends to have his or her own characteristic cycling frequency [18].

4.6. The Willful Choices of the Individual

No two persons are exactly alike. Even identical twins have their own individual likes and dislikes, hobbies and interests, strengths and weaknesses [19]. Although there are many factors that can contribute to these differences, the freedom to choose is likely the most important of them. This freedom affects the way a person perceives, processes, and reacts to various stressors. This in turn influences the way the brain reacts to those stressors, thus explaining how an individual's willful choices can affect the trajectory of FLASH syndrome.

5. Influence of the Neuronal Hyperexcitability Trait on Cognitive, Emotional, and Behavioral Functions

5.1. Cognitive Functions

In the cognitive domain, neuronal hyperexcitability can

cause difficulty concentrating because pathologically hyperactive neurons send too many signals to the mind, and these signals can be distracting. The excess neural signaling can also cause impulsivity if, for example, the mind decides to act on a specific thought or emotion before the brain has a chance to fully process the thought or emotion in conjunction with the mind [4]. In other words, the person may react without fully thinking things through. Affected persons may also be physically hyperactive, as the excess neural signaling floods the mind with ideas that can prompt the person to switch from one activity to another. Taken together, these three potential consequences could account for the triad of symptoms that define attention deficit hyperactivity disorder (ADHD). Additionally, neuronal hyperexcitability can increase the likelihood that various motor programs will be generated either involuntarily or semi-voluntarily, thus explaining the subtle movement abnormalities that can sometimes be associated with ADHD, such as tic disorders and Tourette syndrome.

Another cognitive difficulty that can be caused by neuronal hyperexcitability is inconsistency of cognitive function. At times, for example, the affected person may find that his or her concentration is very good, whereas at other times it may be very poor, even for things that are of personal interest. The MCNH explanation for these shifts in cognitive function is that the hyperexcitable brain is not thought to be hyperactive as a whole; rather, the hyperactivity is thought to occur in the brain's microcircuitry [20], and hyperactive circuits compete for dominance [21]. Hence, when the locus of hyperactivity involves cognitive circuits, cognitive function is apt to be very good; whereas, when the locus of hyperactivity involves limbic circuits, cognitive function is apt to be very poor. That is not to downplay the importance of level-of-interest as a determinant of cognitive function. Catecholamines, which are released more actively when the mind is engaged in things that are interesting, exciting, or alarming, exert modulatory effects in both the prefrontal cortex [22] and the thalamic reticular nucleus [23], thus tending to decrease the amount of electrical traffic that would otherwise tend to cause distractibility. Because this modulatory effect tends to mitigate the waxing and waning of cognitive function that occurs as the locus of hyperactivity migrates from one group of circuits to another, it tends to obscure the fact that cognitive function, like emotional function, tends to wax and wane in persons with hyperexcitable neurological systems.

Other cognitive abnormalities that can be caused by neuronal hyperexcitability include a tendency to over-analyze things, ruminate about things, and obsess about things. All of these phenomena reflect a loss of ability of neurons to self-regulate. Also, because the frequent and repeated stimulation of specific neurons and circuits tends to potentiate their response to further stimulation, the locus of hyperactivity can become stuck in specific circuit loops, thus helping to explain obsessive rumination and obsessive-compulsive symptoms, the latter of which are the prototypical example of this circuit-specific potentiation [24].

In persons with very high levels of neuronal hyperexcitability, even more extreme difficulties in cognitive function may occur. For example, neuronal hyperexcitability may cause a clouding, dulling, or slowing of cognition due to the extraordinary high level of electrical traffic in the brain. Very high levels of neuronal hyperexcitability could also cause perceptual abnormalities, such as auditory and visual hallucinations, if, for example, the locus of hyperactivity were to migrate to circuits that would normally only be activated by sensory receptors in the eyes, ears, and other parts of the body [1].

5.2. Emotional Functions

When the locus of hyperactivity moves to limbic circuits, it could cause the affected person to experience various emotional states, such as anxiety, depression, euphoria, irritability, or various mixtures of these depending upon which specific circuits become pathologically hyperactive at any point in time [1]. The duration of a given emotional state would depend upon the ease with which hyperactive feeder circuits could aberrantly fuel activity in relatively *hypo*active receiver circuits as the feeder circuits waned in activity due to synaptic fatigue [25]. As previously discussed, the latter would depend upon the degree of neuronal hyperexcitability and the degree of connectedness of the neurological system. The higher the level of excitability and the more densely connected the neurological system, the greater the ease with which the aberrant circuit activation could occur. Of course, the locus of hyperactivity would also be influenced by the willful intentions of the individual because specific thoughts, emotions, and intentions stimulate the associated neurons and circuits. This is the MCNH explanation for the cognitive, emotional, behavioral, and functional imaging changes that have been observed with cognitive-behavioral and related forms of psychotherapy. Pitted against this is the tendency for hyperactive neural circuits to draw the cognitive-emotional system into synchrony with them, thereby reducing the affected person's cognitive-emotional flexibility and causing him or her to remain stuck in one cognitive-emotional state or another until the locus of hyperactivity moves to another circuit or group of circuits.

5.3. Behavioral Functions

With all of the aforementioned neurological interference going on, consider how difficult it would be for a person with highly excitable neurons to concentrate on things, make decisions, and figure out how he or she really felt about anything. Normally, the brain is supposed to quietly serve the mind by integrating information and relaying electrical signals between the mind and the body; it is not supposed to be telling the mind what to think, say, or do. Moreover, the neurological interference becomes even more amplified and chaotic when the mind becomes stressed because stress both excites and further increases the excitability of the neurological system. This could help explain why persons with neuronal hyperexcitability may behave in ways that are

overly dramatic, illogical, maladaptive, or self-destructive, particularly when they are under a lot of stress.

From this discussion, it should be apparent that the neuronal hyperexcitability trait can drive any or all of the cognitive, emotional, and behavioral abnormalities that have been described in the wide range of psychiatric disorders that together are referred to as "mental illness." It should also be apparent that mental illness is not the only possible consequence of neuronal hyperexcitability. Some of the other possible consequences—consequences that together with mental illness may help explain why human society is unraveling to the extent that it is—will be discussed next.

6. Other Consequences of the Neuronal Hyperexcitability Trait

6.1. Family Dysfunction

Because neuronal hyperexcitability is an autosomal dominant trait, children who are affected by the trait typically have at least one parent who is affected by the trait. Also, because the trait is additive, those children who are the most severely affected would also be the ones who would be the most likely to have two parents who were affected by the trait. This would create the perfect storm for pathological child development, as those children who were the most emotionally sensitive would also be the ones who would likely be exposed to the highest levels of childhood abuse, neglect, and family dysfunction.

In an effort to shield themselves from the emotional pain, such children are likely to develop defense mechanisms and coping strategies that are tailored more for emotional protection than character development. This is in contrast to unaffected children who, being less emotionally sensitive, would be more willing to bear the emotional discomfort that is often created when one chooses to take responsibility and honor one's conscience. Although there are many other factors that contribute to the development of character flaws and personality disorders, the trait of neuronal hyperexcitability appears to be the most important because a predictable proportion of the children in affected families manage to avoid becoming corrupted by their family dysfunction. These so-called "survivors" almost always appear in an autosomal recessive distribution, suggesting that they did not inherit any of the alleles for neuronal hyperexcitability. An equally predicable proportion of the children in these families appear to be moderately affected, which suggests that they inherited one rather than two of the gene polymorphisms that have been linked to the neuronal hyperexcitability trait [11-14].

6.2. Child Abuse, Neglect, and Poor Parental Role-Modeling

Due to the cognitive-emotional chaos that is wrought by higher levels of neuronal hyperexcitability, affected parents can remain so rapped up in their own emotional angst that they cannot prioritize the needs of their children over their own needs. They may have a mind to be good parents, but their hyperactive brains tend to overpower their minds. Consequently, they have a propensity to use their children, as well as everything else in their lives, to obtain relief from their chronic emotional discomfort. For example, they may have the willingness to do fun things with their children, but only as long as it is fun for them. They may give their children spending money, but only to earn affection from their children. They may give their children the freedom to do whatever they want, but only because they want the freedom to do whatever they themselves want. In more extreme cases, they may use their children to pass lies, assist in illegal activities, or serve as objects of gratification. Conversely, they might be extremely controlling and protective of their children, not so much because they want to protect their children from harm but because they want to protect themselves from the emotional pain that, due to their exquisite emotional sensitivity, they would experience were something adverse to happen to their children.

To observing others, these parenting flaws may seem to be correctable through intensive education and support. However, such a simplistic view would grossly underestimate the power that the neuronal hyperexcitability trait can exert over an affected person's willful intentions. These parents are not just needing skills training and emotional support; they are needing something to quiet their hyperactive brains and relieve their intense emotional suffering. That is why so many of them consume alcohol, smoke marijuana, and use other psychoactive drugs, especially sedating ones. They quickly come to realize that these drugs offer them some relief, even if only temporarily, from the unceasing chatter in their heads and the stormy emotions that they experience. Moreover, even when they do seek mental healthcare, the root cause of their emotional and behavioral problems is seldom addressed because knowledge about the neuronal hyperexcitability trait is just beginning to make its way through the medical field.

6.3. Low Self-Esteem

Untreated neuronal hyperexcitabilty can lead to low self-esteem through a number of mechanisms. To begin with, children who are affected by the neuronal hyperexcitability trait are, as previously discussed, born to parents who are affected by the trait. Hence, in most cases, the parents themselves suffer from low self-esteem, which they tend to pass on to their children through projective identification. Second, the obsessional thinking and emotional angst that are driven by neuronal hyperexcitability tend to prevent affected children from successfully managing the cognitive and emotional challenges with which they are faced. Unaware that their fundamental weakness is much less mental than neurological, they tend to default to blaming themselves or blaming others. Both of these responses have a negative effect on their identity: the former leads to the perception that the self is inadequate, and the latter undermines their relationships, which again leads to a negative self-appraisal.

Third, neuronal hyperexcitability tends to cause restlessness and inattention, symptoms that further reduce self-esteem by thwarting academic success. Fourth, neuronal hyperexcitability commonly drives affected persons to use addictive drugs. This ultimately causes feelings of shame and guilt, particularly if it ends up costing users their jobs or valued relationships. Fifth, affected persons may resort to illegal activities in a desperate effort to maintain housing or support their drug habits. Aside from all the shame that is associated with these activities, various criminal allegations, some of which may lead to arrest, imprisonment, and forced time away from family and children, can deal a particularly damaging blow to their self-esteem.

6.4. Stormy Interpersonal Relationships

As alluded to in the previous section, neuronal hyperexcitability can be extremely damaging to one's relationships. Persons who harbor the neuronal hyperexcitability trait tend to be highly sensitive, reactive, and defensive, all of which can fuel considerable tension when interpersonal conflicts arise. Neuronal hyperexcitability also increases the risk that there will be things to argue about because it tends to drive behavior that is avoidant and self-centered. The risk is even greater with one's committed relationships because emotional and physical intimacy expose one's greatest weaknesses, deepest fears, and most private insecurities. Then, when conflicts arise, even gentle confrontations can rapidly turn into heated arguments because one person's hyperexcitable brain can cause both persons in an argument to escalate. In many cases, both persons in the relationship have hyperexcitable brains, which amplifies the problem exponentially. For all of these reasons, neuronal hyperexcitability is thought to be the primary cause of failed relationships, domestic violence, and other forms of family dysfunction.

6.5. Sexual Promiscuity

In the same way that circuit migration in the hyperexcitability can cause changes in cognitive and emotional function, it can increase or decrease an affected person's libido outside the normal range of variability. Hypothetically, the means by which this occurs is that the locus of hyperactivity can alternate between libidinal and non-libidinal circuits, thereby causing an affected person's sex drive to oscillate from one extreme to the other. The surges in libido can be particularly problematic, especially in teens, who are typically not yet mature enough for a committed relationship. Subsequently, the breakups that they experience can lead not only to intense feelings of grief and abandonment but also to public shame and humiliation, as young persons tend to gossip both verbally and on social media. It can also lead to unplanned pregnancies, sexually transmitted diseases, and crimes of passion. Stressors of this nature are some of the highest, and the emotional pain is abnormally amplified in persons with hyperexcitable neurological systems, thus placing them at elevated risk for depression, psychosis, suicidality, and homicidality.

6.6. Unemployment, Homelessness, and Criminality

The combination of academic, occupational, emotional, and interpersonal difficulties that are fueled by the neuronal hyperexcitability trait can markedly reduce the odds that an affected person will succeed in a highly competitive world. Also, rather than helping to increase motivation, the stress created by falling short of personal and social expectations tends to further diminish the affected person's functional capacity because stress further fuels the fire in the hyperexcitable brain. In the most severe cases, the result is often a downward spiral of stress and more stress that ultimately leads to psychiatric hospitalization, homelessness, or criminality. Virtually all institutionalizations, evictions, and incarcerations are thought to be the consequence of persistently high levels of stress superimposed upon an inherent hyperexcitability of the neurological system.

6.7. Suicidality

Statistics suggest that nearly all persons who commit suicide have a history of either treated or untreated mental illness [26-28]. Mental illness is thought to be rooted in neuronal hyperexcitability. Hence, suicidal thoughts and behaviors are almost always the consequence of untreated or inadequately treated neuronal hyperexcitability.

6.8. Gun Violence and Mass Shootings

The combination of emotional hypersensitivity, mood instability, impulsivity, substance misuse, unemployment, and criminality that are driven by severe neuronal hyperexcitability create the perfect storm for gun violence. In a minority of cases, it can also lead to mass shootings and other forms of terrorism in a brazen effort to retaliate against society for feelings of rejection, alienation, and other painful emotions. Although increasing efforts are being made to regulate the sale of assault weapons, the increasing use of these weapons is a sign of a deeper problem; it is a sign that people are becoming increasingly desperate. Although no single cause of this growing desperation has been identified, there is a general consensus that the level of stress that people are experiencing in modern society is rising [29]. As previously discussed, mental stress, like stones being thrown at a beehive, agitates the brain, and the hyperexcitable brain is like a hive of irritable bees. That makes persons with hyperexcitable brains more vulnerable to stress, and the more stress they experience, the more desperate they become. Although there is no easy way to reduce environmental stress, there is an easy way to reduce neuronal excitability. That makes neuronal hyperexcitability a prime target for reducing gun violence.

It is important to note, however, that the neuronal hyperexcitability trait can be difficult to detect because it is a trait, not a state. That is to say, it is a vulnerability to becoming symptomatic rather than a continuous state of symptomatology. Hence, affected persons may not show any visible signs of the trait until they become sufficiently stressed. Also, because these signs may not be expressed as

classic psychiatric symptomatology, some affected persons might fail to meet diagnostic criteria for a mental illness. In general, symptoms of mental illness are experienced as psychological and emotional distress, and signs are expressed as deficits in functional capacity or oddities of thought and behavior. In some cases, however, the trait of neuronal hyperexcitability might simply be expressed as restlessness, anger, mistrust, excessive worry, or some other cognitive, emotional, or behavioral characteristic that could easily be misattributed to situational factors alone. Also, more typical signs and symptoms of mental illness can be concealed by an individual's decision to keep his or her suffering private and compensate for any lack of functional capacity by relying upon others for help. For all of these reasons, the trait of neuronal hyperexcitability, though being highly ubiquitous, can be very elusive. Fortuitously, however, there is a solution to that problem.

7. Objective Markers of the Neuronal Hyperexcitability Trait

In recent years, an explosion of new research has identified a link between upper-end-of-normal resting vital signs and the later development of various psychiatric disorders and general medical conditions [2]. For example, in a longitudinal study involving more than 1 million men in Sweden, Latvala et al. [30] found that subtle elevations in resting heart rate (RHR) were predictive of the later development of generalized anxiety disorder, obsessive-compulsive disorder, and schizophrenia. Similarly, Blom et al. [31] found that adolescent girls with emotional disorders had increased resting respiratory rates (RRR) in comparison to healthy controls. The general medical conditions with which upper-end-of-normal resting vital signs have been associated include diabetes [32, 33], high blood pressure [34, 35], cardiovascular disease [36, 37], cerebrovascular disease [38, 39], cancer [40, 41], dementia [42], and all-cause mortality [43-46].

The link between upper-end-of-normal resting vital signs, mental illness, and chronic physical illness is thought to be a chronic hyperactivation of the autonomic nervous system as well as other systems of the body, including the cognitive-emotional system, the hypothalamic-pituitary-adrenal system, the metabolic system, and the immunologic system, all consequent to an inherent hyperexcitability of the neurological system [2]. Hypothetically, the reason that psychiatric and functional physical symptoms tend to precede the development of diagnosable medical conditions is that the cognitive-emotional system is more expressive of neuronal excitation than other organs and systems of the body. The physical consequences tend to be delayed because they express the gradual erosive effects of neuronal hyperexcitability [47, 48]. Based on the foregoing observations, which are rapidly being replicated, it has been hypothesized that a resting heart rate above 75 beats/min or a resting respiratory rate above 15 breaths/min is indicative of the neuronal hyperexcitability trait [2].

What makes these findings so vitally important is that they could be offering a simple, objective means by which to detect the neuronal hyperexcitability trait. The ability to detect the trait objectively could circumvent the need to rely solely upon psychiatric signs and symptoms to determine which persons might need medical-psychiatric intervention. It could also be opening the door to a whole new world of prevention—not just of mental illness—but of virtually every medical, social, occupational, and criminal problem with which modern society is being challenged. Through the simple measurement of resting vital signs, carriers of the neuronal hyperexcitability trait could be identified and offered education about the trait from an early age. Beyond that, those with the greatest vulnerability to becoming symptomatic could be offered prophylactic pharmacotherapy. Like pouring a little water on a smoldering flame, prophylactic anticonvulsant therapy, which could more aptly be called "neuroregulator therapy" because of its proposed mechanism of action [49], could prevent cognitive-emotional stress from kindling a fire in the hyperexcitable brain. In so doing, it could prevent the development of the many psychological, emotional, behavioral, medical, educational, occupational, social, and legal problems that have been linked to the neuronal hyperexcitability trait. Never in history has there been such an opportunity to effect meaningful change in the world.

8. Discussion

The purpose of this article was to discuss what is hypothesized to be the biological driver of the multitude of problems that are increasingly disrupting modern society. Based on a rapidly accumulating body of evidence, the underlying driver appears to be a genetically-based hyperexcitability of the neurological system. What makes this discovery so earth-shattering is that the neuronal hyperexcitability trait is highly prevalent, highly detectable, and highly modifiable. Even before symptoms begin, the trait can be detected by simply measuring a person's resting vital signs. Also, because the abnormality is thought to underlie the development of a wide range of general medical conditions irrespective of whether emotionally-distressing symptoms are present, the abnormality could be addressed without incurring the stigma of mental illness. For those affected persons who do experience psychiatric symptoms, targeting the core abnormality of neuronal hyperexcitability, an approach that could be called "focused neuroregulation" [50], would logically be more expedient and effective than the current, symptom-based approach, to treatment. This idea is supported by several observations, which include 1) the well-known benefits of stress-reduction and other natural interventions that have brain-calming effects [51]; 2) the emergent success of ketamine [52] and zuranolone (SAGE-217) [53], two novel brain-calming drugs that have demonstrated more rapid antidepressant effects than traditional antidepressants; and 3) the historical success of benzodiazepine anticonvulsants, non-benzodiazepine

anticonvulsants, non-stimulating antipsychotics, and the anticonvulsant-like drug lithium in the treatment a wide range of psychiatric symptoms. Figure 1 illustrates the response rates to neuroregulators of 258 consecutive inpatients and outpatients presenting to a general psychiatric practice with evidence of neuronal hyperexcitability (as suggested by the instability of their symptoms) [54]. Notably, there was no significant difference in the response rates whether patients had an identifiable history of mania or hypomania (93% response rate) or not (91% response rate). And although some neuroregulators yielded response rates below 50%, the overall response rate to neuroregulator therapy was above 91%. This was made possible by the fact that combining neuroregulators has an additive effect.

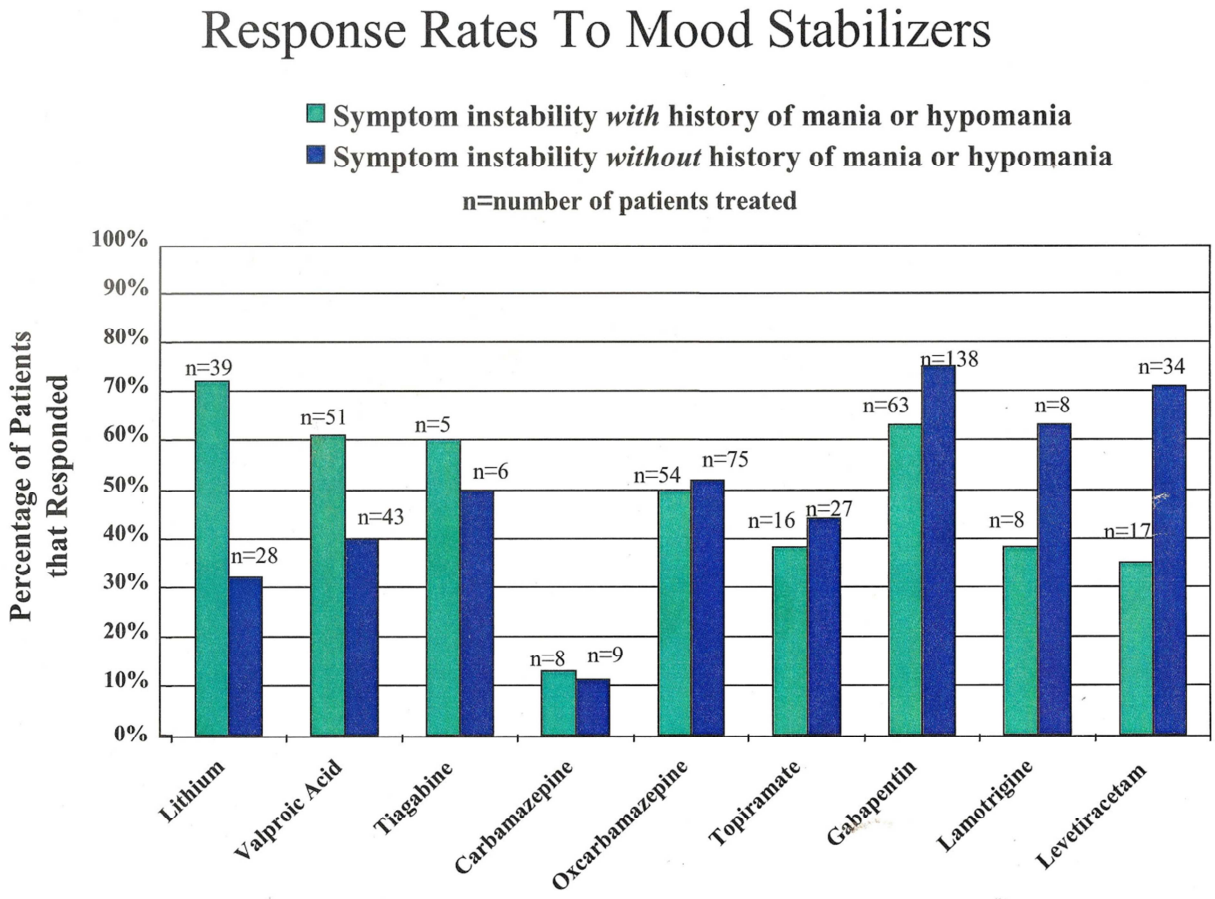

Figure 1. *Comparative response rates to 9 neuroregulators in patients with neuronal hyperexcitability (as suggested by the instability of their symptoms). Green bars indicate a history of mania or hypomania; blue bars indicate no history of mania or hypomania. Notably, these patients made up 95% of 300 consecutive patients presenting with symptoms of depression, and only about one-third among them had an identifiable history of mania or hypomania.*

Table 1 summarizes the impact of focused neuroregulation in comparison to symptom-based treatment.

Table 1. *Clinical outcomes and costs of focused neuroregulation vs. symptom-based treatment in patients suspected of having neuronal hyperexcitability (as suggested by the instability of their symptoms). Estimates are based on more than 20 years of clinical observation and long-term follow-up.*

Outcomes and Costs of Focused Neuroregulation	National Averages
Time to Noticeable Improvement: 3 days	30 days
Degree of Improvement: 80%	50%
Success Rate: 90%	40%
Work Productivity Attainment (10-point scale): 8	6
Quality of Life Attainment (10-point scale): 8	6
10-year Cumulative Service Costs: $6,000	$100,000
10-year Cumulative Medication Costs: $10,000	$100,000
Average Duration of Effectiveness: 20+ years	1 year

Based on these estimates, focusing efforts on identifying and treating the neuronal hyperexcitability trait could provide a cost savings of nearly 50% in mental healthcare alone. With mental illness on the rise in virtually every country in the world, and an estimated cost to the global economy of nearly one trillion dollars annually, that translates to a savings of nearly $500,000,000 each year [55]. Note that this does not include the additional savings that could be had by modifying the neuronal hyperexcitability trait prophylactically. When one considers the reduction in

suffering as well as the many psychological, emotional, medical, occupational, social, and legal problems that could be avoided by reducing neuronal excitability before symptoms begin, the potential cost savings would be astronomical.

These estimates are a trumpet call to action. They are a call to re-evaluate the standard approach to psychiatric care in light of the tremendous utility of targeting what appears to be the core abnormality not only in mental illness but in most general medical conditions as well as the multitude of psychosocial problems that are plaguing our world today.

9. Study Limitations and Directions for Future Research

Although this analysis is based on the latest research studies and more than 20 years longitudinal clinical observations, some of the recommendations remain speculative. Hence, further analysis, including tightly controlled clinical studies, will be needed before its conclusions can be codified and translated into general practice. Specifically, the beneficial effects of anticonvulsant therapy on resting heart and respiratory rate measurements will need to be studied more formally and with larger sample sizes before recommendations for anticonvulsant prophylaxis can be made. Also, all-member family studies will be needed to verify the hypothesis that those family members who grow up mentally and emotionally healthy and, thus, would be presumed to have *normo*excitable neurons, actually have significantly lower resting vital-sign measurements than their affected siblings. Finally, long-term prospective studies will be needed to determine the psychosocial, occupational, and medically-protective effects of neuroregulator prophylaxis.

10. Conclusion

Most healthcare experts agree that prevention is the way of the future. But until now, most of the widely prescribed preventive measures, such as beta blockers to prevent cardiac arrhythmias, statins to lower cholesterol, and anticoagulants to prevent blood-clots, have been directed at preventing the further progression of disease. Strikingly, the only truly preventive measures, which include stress-reduction, minimization of refined sugar, and moderate exercise, have the shared effect of calming the brain. Unfortunately, however, these interventions, though widely applicable, are rarely implemented by those who need them the most; namely, persons who inherit the genes for neuronal hyperexcitability. The reason that such persons rarely implement these strategies is that the mind of the affected person is often too weak to adequately govern the hyperexcitable brain. Indeed, one of the hallmarks of neuronal hyperexcitability is a lack of self-discipline. The good news, however, is that an entire class of neuroregulators is currently available, and the prophylactic use of these drugs could calm the brain enough to allow affected persons to implement the aforementioned natural interventions routinely. Until now, these relatively safe and inexpensive drugs have primarily been used to treat epilepsy. However, their brain-calming effects are even better suited to prevent the wide range of psychiatric, medical, and social problems that have been linked to neuronal hyperexcitability because, unlike most persons with epilepsy, most persons with neuronal hyperexcitability do not have the added complication of a structural brain abnormality. And although these drugs have been used in psychiatry for more than fifty years, the inability to visualize the core abnormality in mental illness has left them sorely underutilized. This presentation is a trumpet call to announce the golden opportunity that we have to change the world through a widely available, largely untapped, inexpensive resource.

Competing Interests

The author declares that he has no competing interests.

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