

LYME NEUROBORRELIOSIS & AGGRESSION

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Summary:

The link between Lyme neuroborreliosis (LN) and aggression is reviewed from multiple perspectives. Cases are presented and discussed. It appears Lyme disease (LD) and other related tick-borne diseases contribute towards causing human aggression and violence. Greater attention to this area has the potential of reducing crime and saving lives. Narrow and restrictive opinions on the diagnosis and treatment of Lyme disease can contribute to the increased consequences of late stage disease, which includes aggression and violence associated with Lyme disease and other related tick-borne diseases.

Background:

Lyme disease (LD) is a multi-systemic disease with a predominance of dermatological, musculoskeletal and neuropsychiatric symptoms. Predominant symptoms are first dermatological, then musculoskeletal, and finally involve the central nervous system (CNS) in late stage disease. These symptoms may be cognitive, psychiatric and other neurological impairments. Late stage LD, with a predominance of cognitive, psychiatric and neurological symptoms has been called many different names throughout history and in different geographical regions. Recently used terms include Neuropsychiatric Lyme disease, Neurolyme, Lyme Encephalopathy and Lyme neuroborreliosis. The causative agent of LD is *Borrelia burgdorferi* (Bb.), a spirochete, with many similarities to syphilis. Since vectors which transmit Bb. are often infected with other microbes, an infection with Bb. is sometimes complicated by other tick-borne pathogens. Interactive copathogens are more common in more severe and more chronic cases.

Although aggression is a normal human function, dysregulated aggression causes violence, which does not facilitate adaptation and poses a major threat to individual health, social stability and the survival of our species. Pathological aggression and violence are not a result of any one cause. Instead, it is a result of a combination of contributors to violence, which are not adequately compensated by the deterrents to violence. Many of these contributors are unknown and others have described some (1,2,3,4,5). This paper shall focus upon a contributor, which has not been the subject of a large amount of research in the past, the role of infectious diseases, and more specifically tick-borne diseases and LN.

Method:

The author has treated a significant number of patients in whom there is an apparent association between LN and violence or symptoms associated with violent potential. A series of 20 of these cases are reviewed and representative cases are described. In addition, historical references are

considered, epidemiological patterns are discussed, the medical literature is reviewed and pathophysiology is discussed. Treatment issues and advocacy issues are also addressed.

Results:

The evidence to support the view that LN is a contributory factor in causing violence is drawn from a combination of case histories, theoretical biology, historical references, epidemiological patterns, a review of the medical literature and pathophysiological considerations.

Case Histories:

Case 1:

A 14 year old white male with a history of Bb. demonstrated aggressiveness. The patient may have had congenital exposure to LD, there is a history of multiple tick bites and there were bull's eye rashes on two separate occasions at ages 6 and 8. His most notable symptoms include difficulty sustaining attention, being easily distracted by frustration, olfactory hyperacusis, stuttering, intrusive images, hypnagogic hallucinations, apathy, decreased frustration tolerance, sudden abrupt mood swings, disinhibition, exaggerated startle reflex, explosive anger, violent outbursts, being accident prone, decreased school performance, disruptive behavior, depression, not being well rested in the morning, insomnia, hypersomnia during the day, intolerance to heat, conjunctivitis, dizziness, motion sickness, joint pain, crepitations, sore throats, and irritable bowel syndrome.

These symptoms progressively evolved over time. The aggressive tendencies were of particular concern; as the patient would repeatedly attempt to choke his mother to death, destroy his house, knock over furniture, and kick and punch holes through walls and doors. Frequent police intervention was needed. One experienced officer said it was the most violent teenager he had ever seen. There was a troubling lack of empathy and a lack of remorse for his behavior.

Laboratory finding demonstrated positive findings on the Lyme IgM, Lyme IgG, Lyme PCR (urine), HHV-6, Bartonella (blood and spinal fluid), and stealth virus culture. The PET Scan demonstrated a slightly heterogeneous uptake of radiotracer with foci of mild hypermetabolism in the left parietal and bilateral medial temporal lobes. An MRI was normal.

The patient was treated with a number of different psychotropics and antimicrobial strategies. He is currently showing a partial response to a combination of Famvir 500 mg tid, Claforan 3 gm bid, Zithromax 500 mg bid, Risperdal 5 mg bid, Concerta 18 mg qam and 5 mg late afternoon. Whenever the antibiotics are stopped, the patient becomes quite aggressive. This is especially true with the Famvir, which results in increasing irritability and aggressiveness within 24 hours whenever this is discontinued.

Case 2:

An 8 year old male complained of leg pains, and testing for LD was negative. Three years later there was a physician observed and documented 18 cm. bulls eye rash accompanied by a flu-like

illness. It was treated with a brief course of Doxycycline. Then, there was the gradual development of a number of symptoms that included decreased attention span, auditory hyperacusis, decreased ability to remember people's faces, decreased concentration, spelling errors, decreased reading comprehension, decreased frustration tolerance, irritability, sudden abrupt mood swings, explosive anger, suicidal and homicidal urges, depression, mood swings, intrusive and obsessive thoughts, compulsions, anhedonia, nightmares, insomnia, anorexia, headaches, blurred vision, eye pain, dizziness, muscle tremors and twitches, a burning sensation in his feet, social isolation, fevers, sweats, chills, sore throats, coughing, heartburn, chest pain, shortness of breath, stiffness of joints, fatigue, episodes of destructive episodes that could last about one hour and fire setting.

Positive laboratory findings included Lyme Western Blot, Babesia microti, Human Granulocytic Ehrlichiosis, Human Monocytic Ehrlichiosis and stealth virus.

There were multiple suicide attempts and one serious homicide attempt. He demonstrated partial improvement from a combination of Paxil, Depakote and an extended course of antibiotics.

Case 3:

A 27 year old male gradually began developing a multi-systemic illness 9 years ago. He was diagnosed with LD 7 years ago, and has had courses of antibiotic treatment since the initial diagnosis. A multitude of cognitive, psychiatric, neurological and somatic impairments associated with LD and LN were present including symptoms associated with attention span; allocation of attention; distraction by frustration; distraction by hyperacusis to auditory, visual, tactile and olfactory sensory input; working memory; working spatial memory; recent memory; encoding errors; slowness in retrieval of words, numbers, motor sequences and geographical memory (driving to the store); letter reversals; spelling errors; number reversals; reading comprehension; optic ataxia; calculation; fluency of speech; slurred speech; stuttering; handwriting; depersonalization; intrusive aggressive and sexual images; hypnagogic hallucinations; vivid nightmares; sleep paralysis associated with horrific nightmares; illusions; auditory visual and tactile hallucinations; unfocused concentration; "brain fog" sensation; inability to prioritize multiple tasks; poor concentration on multiple simultaneous tasks; racing thoughts; obsessive thoughts; mental apathy; poor abstract reasoning; decreased frustration tolerance; sudden abrupt mood swings; paranoia; disinhibition; explosive anger; feeling suicidal and homicidal; accident proneness; decreased social functioning; disability; disassociative episodes; compensatory compulsions; dropping objects, depression; panic disorder; obsessive-compulsive disorder; social phobia; generalized anxiety; not being rested in morning; early, mid and late insomnia; hypersomnia; loss of normal 24 hr. circadian rhythm; anorexia; weight loss; episodes of over-eating and weight gain; increased libido; decreased capacity for pleasure; altered sexual imagery; body temperature fluctuations; flushing; intolerance to heat and cold; decreased body temperature; low grade fevers; night sweats; chills; headaches--cervical radiculopathy, migraines, orgasm induced migraines, TMJ, tension, cluster and sinus; loss of smell; blurred vision; sensitivity to bright, fluorescent & flickering lights; floaters; dry eyes; night blindness; peripheral shadows in visual fields; heat wave-like visual distortion; double vision; ptosis (L); loss of sensation on the side of the face; Bell's palsy; drooling; tinnitus; hearing loss; dizziness; loss of speech; difficulty swallowing; sternocleidomastoid and trapezius

pain and paresis L>Rt.; tongue deviates to L side; numbness; tingling; sensory loss; burning; static electric sensation; crawling sensation under skin; stabbing sensation; paresis; tremor; twitching; muscle tightness; restless leg; myoclonic jerks; herniated disks lower back (No trauma); meningismus; positive Romberg; swelling, pain and tightness in multiple joints; periostitis of tibiae, ribs, Rt. iliac crest, sternum and clavicles; epicondylitis; plantar fasciitis; chronic fatigue syndrome; fibromyalgia; myalgia; chondritis of ear and nose; chest pain; racing pulse; episodes of rapid and slow heart rate; shortness of breath; sore throat; swollen glands; non-ulcerative dyspepsia; abdominal bloating; irritable bladder; episodic dysuria; hypoglycemia; tooth pain; allergies; ecchymoses; and chronic pain.

Positive laboratory findings included Lyme PCR, Lyme Western Blot on multiple occasions and Babesia microti.

The patient described intrusive, overpowering very violent thoughts. At times, the intrusive, violent, thoughts would be triggered by stimulation; such as a dog barking, a bird chirping, a strobe light or the presence of other people. There were also episodes of anger with an urge to destroy. He described sudden urges to rip the room apart and kill everyone and every animal in the house. At times, he has obsessions that he wished he had an excuse to go after someone. The patient is particularly frightened when he has these urges in the presence of children. He felt he could sometimes stop these urges by hurting himself. Sometimes the aggressive urges changed to panic, fear of death and death wishes. There were rapid mood changes. He described road rage out of nowhere and fantasies of beating and killing people. His wife also has LD and LN, and has also experienced suicidal and homicidal urges as a part of her illness. Some of the symptoms responded to antibiotic treatments. The aggressiveness persisted, but is responding to a combination of Zyprexa and Depakote ER.

Case 4:

A 29 year old female with clinical symptoms compatible with the diagnosis of LN and positive reactivity on the Western Blot (5 bands on the IgG) was treated with extended courses of oral antibiotics, which helped many other symptoms of LD and LN. However, aggressive and homicidal urges, contrary to her normal personality, persisted years after her initial antibiotic treatment. The patient described episodes of fear, anger, depression and/or extreme social anxiety that would occur suddenly and totally unprovoked. She would look at someone, and feel anger for no reason whatsoever. For example, once she looked at a woman in a restaurant, and had an urge to hurt her. At other times, there would be sudden and unprovoked urges to harm family members. These episodes would sometimes be preceded by feeling a sense of derealization, dizziness, impaired concentration, decreased spatial memory (i.e. could not remember her mailbox), weakness in her legs and she reported generally feeling "out of it." Then, the bizarre, uncontrollable, racing thoughts and urges would occur. The patient would then feel very upset and frustrated with herself that she felt this way. The episodes could persist hours or as long as an entire day. These symptoms became worse after minimal alcohol intake and were also increased by antidepressant treatment. Occasionally, the patient would wake up experiencing one of these episodes. On one occasion, she woke up screaming. On other occasions, she woke up with an urge to hurt a family member with whom she has a good relationship. The patient was particularly afraid of the episodes during the night, since she had

less capacity to suppress these destructive urges and to restrain herself while still half asleep. One EEG was performed, which was normal. The current treatment is Provigil and Zyprexa p.r.n.

Case 5:

A 40 year old female with a history of tick bites over a span of time has a multitude of cognitive, psychiatric, neurological and somatic symptoms associated with LD and LN similar to those described on the other cases. Positive laboratory testing included Lyme PCR, multiple Lyme Western Blots, Babesia microti, Bartonella and Ehrlichia.

She described her aggressiveness in the following words:

“I am a forty year old woman, and I have had chronic Lyme Disease for years. Throughout this battle, there are two symptoms that scare me to death. One is my suicidal rage and the other is homicidal rage. I have rage that comes out of nowhere and takes over my whole body. It is worse when I am driving. There was one day in particular, I was driving through my town and a garbage truck cut me off. I became so enraged that I followed him to the place where he works, honking my horn and yelling. When I reached his office, I got out of my car and went inside pointing and yelling in the driver’s face. There were three other men in the office, and they were all looking at me as if I was crazy. I was so crazed, I wanted to jump over the desk and choke the man. I returned to my car in amazement that I wasn’t hurt. I thought to myself that I must be crazy. When I am on the road, I am very scared for the people who come in contact with me. Because I become so angry over simple things when I am driving, I am sometimes hesitant to get behind the wheel. I don’t know where all of this madness comes from. It’s something I have no control over. Not only am I homicidal, I am also suicidal. There are days that I think about killing my ex-husband and my son, and then myself. Last year, I was planning on going across the street from my house to the hunting field. I wanted to dress as a deer so a hunter would shoot me. I have all these sick thoughts, and they appear out of nowhere. I call companies and scream at them for tiny mistakes. I feel like a mad woman. I think my suicidal thoughts are especially prevalent when I have panic attacks, which are quite often. The panic attacks are just another symptom of Lyme. Everyday I live with these sick thoughts in my head. There is so much more that I can’t even express. I have had these thoughts for the past few years, and I am afraid they will get worse. I feel like I should put a sign in my car--‘Caution.’ I live with this fear everyday, that I might get worse. I have just another reason to thank Lyme disease for my wonderful life.”

Discussion of Case Histories:

In addition to the symptoms described in these cases, other aggressive symptoms I have observed in association with LN include homicide, suicide, combined homicide and suicide, assaults with guns, assault with a knife, assault with a sword, assault with an axe, assault with a hammer, assault with rocks, assaulting a sibling’s head with a rock, pedophilia, stalking, child abuse, assault towards teachers and other students, assaults at summer camp, self inflicted injuries, other types of road rage incidents, domestic violence, torturing household pets, killing pets, armed robbery, shoplifting, destroying property with total amnesia of the event afterwards, breaking

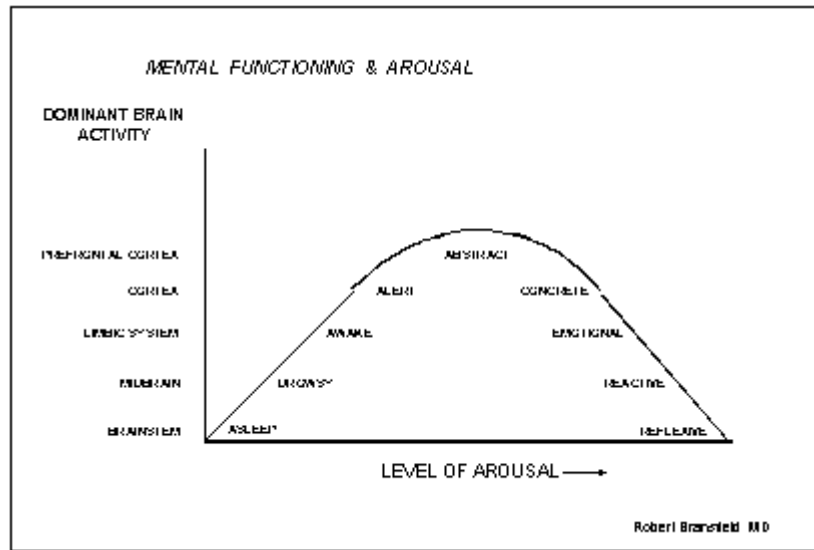
and attempting to break automobile windshields and various forms of public lewdness.

After reviewing these and other cases of aggression associated with LN, there are a number of different patterns that are apparent. In general, the aggression is bizarre and senseless. It is often unprovoked, but sometimes provoked by minimal stimulation. There is a paroxysmal and seizure-like quality to these episodes. Some commonly prescribed medications, sleepiness and fatigue contribute to increasing the risk of these episodes. It should be noted that LD patients sometimes have unusual reactions to medications. Amnesia is sometimes a part of these episodes. Children and teenagers have less insight, and are more prone to act out in an aggressive manner. Adults generally, but not always, have more insight and resources to deter acting on these aggressive urges and intrusive thoughts.

Symptoms associated with LN that may contribute to increasing risk for aggression include—sensory hyperacusis, significant cognitive impairments, decreased visual memory, impaired ability to recognize faces, depersonalization, derealization, intrusive images and thoughts, horrific nightmares, illusions, hallucinations, decreased or lack of empathy, low frustration tolerance, hypervigilance, acoustic startle, paranoia, irritability, sudden abrupt mood swings, disinhibition, explosive anger, suicidal tendencies, homicidal tendencies and substance abuse. The inability to remember people's faces appeared to be associated with predatory aggression. Patients demonstrating aggressive tendencies often had indications of the presence of other interactive co-pathogens, which included Babesia, Bartonella, Ehrlichia and viral infections.

In a state of health, mental functioning facilitates adaptation and there is the capacity to pursue productive activities and relationships and the flexibility adapt to change and adversity. A healthy individual, in a state of full alertness and moderate levels of emotional arousal, is able to mobilize their higher powers to exert willful and knowing control over the more primitive and powerful lower mental functions (diagram). The highest and most uniquely human adaptive capabilities are in the anterior regions of the frontal and temporal lobes. Infectious diseases can cause trauma and dysfunction of different brain regions, which contributes to a large spectrum of mental dysfunction. The location and nature of the dysfunction will contribute to determining the nature of the mental symptom and syndrome. Dysfunction of different pathways in the hierarchy of neural networks that control aggression can contribute to dysregulated aggression and violence. When this is seen, lower power functioning can be dominant over the higher powers, as would be normally seen on either end of the curve only in very low or very high levels of emotional arousal (diagram).

Slide 1



Theoretical biology:

Many diseases, which could not be understood previously, are now better comprehended when we consider the role that microbes often contribute to the disease process. Although we see ourselves as the dominant species on this planet, others may note the lowly microbe may be the dominant species of our biosphere. There is considerable evidence that microbes manipulate the behavior of their hosts to benefit their survival and reproduction. Microbes cause us to sneeze or have diarrhea, which facilitates their propagation. In addition, more complex behavioral changes have been noted with recent research. Wolbachia changes the host's reproductive capabilities; Malaria causes the host to be prostrate and more vulnerable to subsequent mosquito bites, thereby causing further parasitic dissemination; and Toxoplasmosis promotes propagation by causing the host to be more vulnerable to being victims of predators (6,7,8).

Some of the diseases associated with behavioral changes are zoonotic diseases, where microbes complete different parts of their life cycle in different hosts. Mammals, other than man, are more commonly a part of their normal life cycle. Man may sometimes be an accidental host in this zoonotic cycle. When these diseases are considered from the perspective of a zoonotic process; there may be adaptive value for the parasite to cause the host to become more aggressive, sexually aggressive, predatorial, and/or more vulnerable to victimization.

We need to explore the possibility whether tendencies for humans to become a predator and/or a victim may have an infectious disease component which can be sexually transmitted and/or transmitted as zoonotic diseases.

Historical References:

A number of relevant historical references draw an association between Neurosyphilis and violence. There are many similarities between the neuropsychiatric manifestations of Syphilis

and Lyme disease. In addition to the citations in the medical literature, there are references in literature, and a number of famous and infamous individuals noted for their violent tendencies were considered to possibly have syphilis. These individuals include Peter the Great, Henry IIX, Idi Amin, Al Capone and questionably Adolf Hitler.

Cannibalism has been present in different cultures throughout history and is seen in one third of serial killers. It is very difficult to comprehend what motivates this bizarre behavior. Could a zoonotic disease ever contribute to causing cannibalism?

Throughout history, soldiers returning from foreign wars often returned with new and unusual diseases. These diseases were often difficult to understand, but often showed patterns suggestive of infectious disease. Could these diseases have contributed to the wars they were returning from?

Epidemiological Patterns:

There are certain regions of the world that appear to be endemic to violence. Wars, rape and other violence and atrocities in these regions are often considered to be a result of cultural, religious and ethnic intolerances. However, people from these same diverse backgrounds live in greater harmony in other parts of the world. Conversely, there also appears to be regions of the world in which there is a minimal degree of violence. Most infectious diseases show geographical patterns. Two areas of the world endemic for violence are the Middle East and the Balkans. The Balkans is known to be endemic for LD, and a number of soldiers and civilians who have returned from Bosnia are infected with LD.

Review of Medical Literature:

Although there are no prior articles in the peer-reviewed literature devoted exclusively to the subject of LN and aggression, there are a number of references on this subject within the peer-reviewed literature and within presentations at national and meetings (9,10,11,12,13,14).

There are citations documenting the link between violence and a number of infectious diseases that affect the brain (15,16,17,18). In addition, there are citations documenting the causal relationship between syphilis and violence (19,20). Syphilis is a spirochetal disease that is very similar to LD. Also there are citations demonstrating the causal association between cerebral malaria and violence (21,22). Malaria has many similarities to Babesiosis, a tick-borne disease that frequently is an interactive infection, which is often present in patients with LD. Animal studies have demonstrated personality changes associated with *Babesia microti* infections (23, 24). In addition, there is research demonstrating that Toxoplasmosis infections in man alters personality by decreasing superego strength (25,26,27). A reduced superego strength in humans demonstrates some similarity to the animal findings, where infection is associated with increased vulnerability for predation.

There is an association between violence and other conditions that result in dysfunction of the CNS, such as dementia (28,29,30,31). There are also some findings that LN may contribute to

some of the clinical presentations that are sometimes diagnosed as dementia (32,33).

Pathophysiological Considerations:

LN is one of many infectious and immune mediated pathophysiological processes that contribute to diseases and mental illnesses. This term is an acronym that can be abbreviated as "IIMPP."

Although it is clear that Bb. causes considerable neural dysfunction, the exact pathophysiological process is a subject of current research. Proposed pathological mechanisms which contribute to the neural dysfunction associated with LN include vasculitis, direct cell penetration, toxin release, cytokine effects, inflammation and excitotoxicity mediated by quinolinic acid and kynurenine (14).

Adequate conversion of tryptophan into serotonin within the CNS is considered to be highly significant for emotional stability. Depression, suicide, violence, obsessive compulsive disorder and fear and anxiety disorders are associated with reduced serotonin levels. It has also been demonstrated that reduced levels of 5-HIAA (a metabolite of serotonin) in the cerebral spinal fluid is associated a high risk of suicide attempts and impulse control disorders in convicted murderers (34).

There appears to be reduced conversion of tryptophan into serotonin within the CNS in a number of infectious diseases that affect the brain, including LN (35). Instead of converting to serotonin, there is increased conversion of tryptophan into quinolinic acid and kynurenine in LN (36). These two alternative metabolites of tryptophan are excitatory, and can contribute to excitatory neurotoxicity. In an animal model, kynurenine and quinolinic acid caused behavioral shifts associated with aggression, consisting of limb hyperkinesis, emotional strain, malice, fear, aggression with snarling and hissing and attack on provocation. It was suggested by the authors that kynurenines and quinolinic acid can participate in the generation of disorders peculiar for epilepsy (37).

Discussion:

Since violence is determined by a combination of many contributors and failures of deterrents, a complex approach is needed to understand the multiple determinants that contribute to, or deter violence. The author treats many patients with LN, and has noted that a small, but significant percentage of these patients describe similar problems with an onset of aggressiveness associated with the progression of their illness. Most commonly, patients describe decreased frustration tolerance, irritability, and some explosive anger; however, a lesser number experience more severe episodes of rage and other forms of aggressive behavior. Patients frequently refer to this symptom as "Lyme rage." Most commonly, these episodes occur within the home, and do not result in legal charges; however, some of the more severe cases come to the attention of the legal system. Most often, these cases involve domestic violence complaints, but they may also include episodes of "road rage," shoplifting, child abuse allegations, assaults, pedophilia, filicide and other homicides.

These patients respond to treatment with antibiotics and psychotropics. Antibiotic treatment

can cause an initial increase of aggressiveness as a result of the Jarish-Herxheimer reaction (9,37). Adequate treatment for LN, however, is sometimes difficult for patients to access as a result of some highly restrictive opinions on the diagnosis and treatment and diagnosis of LD (38). It is important to recognize that opinions on treatment guidelines for Lyme arthritis should not be used as guidelines for the treatment of LN, or LN where violent potential exists. Due to the complexity and our limited understanding of this disease and the complexity and our limited understanding of human mental functioning and violence, it is impossible to create rigid diagnostic and treatment guidelines at this time. Diagnostic and treatment suggestions for LN have been presented throughout the psychiatric literature and at various national and international meetings (9,10,11,12,13,14).

A database of patients with LN is currently being established to better organize the symptoms and laboratory data associated with patients with LN.

Conclusions:

Based upon the information reviewed in this article, LN appears to be one of many factors that contribute to human violence. Violent behavior associated with LN tends to be bizarre and senseless in appearance. Information from a number of different sources supports, but does not prove the association between LN and pathological aggressiveness. Most patients with LD and LN are not violent, however a small percent demonstrate different degrees of aggressiveness. This may include relatively mild symptoms such as reduced frustration tolerance and irritability. In more extreme and relatively rare instances, there may be explosive anger (sometimes called Lyme rage), decreased empathy, suicidal tendencies, suicide, interpersonal aggressiveness, homicidal tendencies, predatory aggression and homicide. Further research is needed to further explore the association between LN and aggression.

When aggressiveness is associated with LN, antibiotics are an additional and effective treatment option when combined with other psychiatric interventions. Since this is an additional consequence of the underdiagnosis and the undertreatment of Lyme disease, further education to increase the effectiveness of the diagnosis and treatment of LD is suggested. The presence of an infectious disease whether it is Bb. or some other pathogen, which contributes to violence in a powerful and influential individual can have serious adverse consequences if not adequately diagnosed and treated. In our current society of high tech weaponry, it is not just world leaders, but also many other individuals who can have a highly destructive effect upon our global community.

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