

Delving into Neurogenesis of Intermittent Explosive Disorder

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Abstract

Human violence is a complex act that involves harming oneself, others, or objects physically or verbally. It takes on many forms and can be protective, planned (e.g., predatory), or impulsive (non-premeditated). In contrast to deliberate and impulsive aggressiveness, which are seen as unhealthy, defensive aggression falls within the normal range of human behaviour. However, a convergent pattern of data consistently connects impulsive, but not deliberate, aggression to biological, environmental, pharmacological, and psychological treatment response characteristics.

Keywords: IED definition • Neurogenetics • Substance use disorder • Neurobiological assests

Introduction

IED, or intermittent explosive disorder, is a mental illness marked by frequent bursts of impulsive, aggressive, and violent behavior. IED sufferers may find it difficult to manage their anger, which can lead to aggressive behavior towards others or towards things, whether verbally or physically. These outbursts, which are frequently out of proportion to the circumstances and may cause physical harm or property damage, are not always justified.

There is evidence connecting numerous reward genes with dopaminergic activity to undesirable explosive, violent, and aggressive behaviors [1]. For those who provide mental health care, violence and aggression present both a difficult therapeutic challenge and a serious public health issue [2]. The aggression trait is known to have a variety of polymorphic genetic antecedents, variable neuroanatomy, altered regional volumes, and abnormal interregional connections [3]. Understanding the neurogenetics and neurobiology of the reward circuitry in the brain (i.e., serotonergic, cannabinoid, opioidergic, GABAergic, glutaminergic, and dopaminergic, etc.) offers clinically relevant targets for potential therapeutic intervention, including early detection of aggressive behavioral risk. It is remarkable that the number of our youth who experience disciplinary or legal issues as a result of violent or aggressive behavior has exploded. A pattern of recurring angry outbursts within a year is reported by 17% of teenagers and approximately 8% of adults. These people exhibit substantially higher levels of aggression and impulsivity than nonaggressive controls. Additionally, they are more likely to be detained by law enforcement, possess and use firearms, threaten others, commit intimate partner violence, and threaten others [4]. As a result, society bears a heavy financial and social cost as a result of aggressive and violent people. Additionally, those who experience sporadic rage attacks are hesitant to get help, particularly if the episodes are followed by physical violence [5]. Teenagers have recently become more proficient at using and accessing new media technology, such as cell phones and laptops for internet access. Both potential advantages and risks come with this technology surge [6]. Teenagers

should be aware that the likelihood that they will experience peer antagonism through these channels is growing.

Relating Substance Use Disorder (SUD) with IED

IED (intermittent explosive disorder) is the only psychiatric diagnostic for which affective violence is the main symptom [7]. We are aware that a diagnosis of Alcohol Use Disorder (AUD) and a history of abuse as a kid raise the risk of getting IED. Additionally, there is a link between AUD and childhood abuse as well as an increase in overall aggression, including aggression while inebriated. Puhalla, et al. analysis found that IED status was predicted by childhood abuse rather than AUD status. IED, aggressiveness frequency, AUD, and childhood abuse were all independently linked to overall aggression, according to research by Puhalla, et al. However, only those with IED demonstrated increased inebriated aggression in relation to the severity of their AUD. So one potential neurological underpinning for this kind of behaviour could be hereditary susceptibility. For instance, a history of maltreatment during infancy may raise the likelihood that an individual will act aggressively in general and acquire an IED, which may strengthen the link between the severity of SUD and well-known drunken aggressiveness.

Understanding the connections between aggression, rage, violence, alcohol, and drugs is crucial. Anger is associated with relapse, according to terminology used by Alcoholics Anonymous [8,9]. Clinically, anger and violent outbursts, for instance, could be symptoms of attention deficit disorder, bipolar disorder, posttraumatic stress disorder, antisocial, borderline, and paranoid character abnormalities. The harmful effects of stimulant substances like methamphetamine and cocaine cause hyperactivity and anxiety in terms of psychopharmacological mechanisms. In addition, abuse and violence are the primary causes of death for addictions to stimulant drugs [10,11].

Neurogenetics of IED

Since ancient times, there has been a great deal of interest about the causes of human aggression [12]. For instance, aggressive behaviour and the possibility of being born a "natural killer" raise concerns about the nature/nurture dilemma. We are aware that the phenotype of IED is influenced by both the influence of epigenetics and inborn genetic polymorphisms. Specific DNA variants that increase the risk for violent and antisocial behaviours have been found by several studies. The conclusion that significant genetic diversity in aggressive and antisocial behaviour is caused by genetic factors is supported by evidence from behavioral genetics. In a meta-analysis, found that genetic factors could account for 56% of the variance in antisocial behaviour, with 31% owing to particular non-genetic factors and 11% related to shared non-genetic factors. Ferguson contends that the outcomes provide evidence of an association with evolutionary psychology. The idea that a sizable portion of the diversity in Antisocial Personality and Behaviour (APB) is related to hereditary influences is supported by data from behavioural genetics. Many scientific disciplines, including psychology, medicine, and criminal justice, find it difficult

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to apply this knowledge to earlier paradigms that only addressed the acquired or extrinsic causes of antisocial behaviour. Ferguson offers a meta-analytic overview of research on the behavioural genetic causes of APB. Findings showed that genetic factors can account for 56% of the variance in APB, with 11% of the variance owing to shared non-genetic influences and 31% of the variance due to unique non-genetic influences. The mechanistic understanding of brain function relies substantially on neuronal membrane potential. Targeting fluorescently labelled neurons with whole-cell recordings and two-photon imaging reveals cell type-specific membrane potential dynamics of retrogradely or genetically labelled neurons. Dual whole-cell recordings show *in vivo* behavioural modulation of synaptic transmission characteristics and membrane potential synchrony. Whole-cell recordings and optogenetic manipulations can be combined easily to provide precise information about the impact of various perturbations on the membrane potential of various types of neurons.

Additionally, certain genes connected to the underlying biochemical processes that underlie aggression in animals share similarities with the arrangement of relevant physiological processes in humans. As a result, we will give a brief overview of the many functions of "reward" genes and related addiction risk polymorphisms in IED, especially in humans, in the section that follows. We propose that categorising distinct types of impulsivity and impulsive behaviours in relation to these genes may advance our comprehension of the neurological bases of illnesses where impulsivity is a feature. IED and other aggressive and violent behaviours linked to other psychopathologies are examples of these disorders. Finally, we incorporate impulsivity and all these interacting variables into the model depicted in figure 1.

Factors responsible for causing IED

IED's precise causes are not entirely understood, but research indicates that a confluence of genetic, biological, and environmental elements may play a role in its emergence. Serotonin, a neurotransmitter that controls mood and behaviour, may be present at reduced levels in people with IED.

Genetics: IED may have a hereditary component, according to data that it runs in families. Specific genes that may be linked to an elevated risk of violent behaviour have been identified through studies.

Brain chemistry: Abnormalities in brain chemistry, such as imbalances in neurotransmitters like serotonin, dopamine, and norepinephrine, have been linked to aggression and impulsivity, which are key features of IED.

Trauma and stress: IED risk may be increased by childhood trauma, such as physical or mental abuse or exposure to violence. Chronic stressors including financial hardships, interpersonal conflict, or work-related stress may also play a role in the disorder's development.

Substance abuse: Abuse of drugs and alcohol, especially alcohol and stimulants, has been associated with an increase in impulsivity and aggression and may make IED symptoms worse.

Personality factors: Particular psychological traits, such as severe hostility or impulsivity, may increase the danger of IEDs.

Environmental factors: IED development may be influenced by environmental variables such exposure to violence, poverty, and social isolation.

Psychological correlates vs. neurobiological assets

Beyond the usual markers of physical or verbal violence and impulsivity, intermittent explosive disorder (using research definitions) is associated with increased scores on a number of psychometric tests. High levels of relational violence are observed in those with the condition, which suggests that violent impulses can extend to behaviour intended to sabotage interpersonal relationships. Individuals with intermittent explosive disorder (research criteria) also exhibit greater hostile attribution bias, greater negative emotional responses to socially ambiguous stimuli, greater affective lability and affective intensity, and a greater degree of immature defense mechanisms, such as acting out, dissociating, and withdrawing from others, suggesting a psychological mechanism that causes impulsive aggressive outbursts.

While studies on aggression and specific brain chemicals, such as serotonin, clearly demonstrate a biobehavioral link, studies on intermittent explosive disorder have just recently been undertaken. According to research criteria, subjects with intermittent explosive disorder have different serotonin functions from those without the disorder or healthy control subjects; they also have fewer platelet 5-HT transporters and a smaller prolactin response to d,l-fenfluramine and to d-fenfluramine. Furthermore, in patients with personality disorders who met research criteria, two studies using Fluorodeoxyglucose (FDG) Positron Emission Tomography (PET) reported low FDG utilisation after d,l-fenfluramine challenge in frontal areas of the brain and low FDG utilisation after m-chlorophenylpiperazine challenge in the anterior cingulate in the patients with personality disorders who met research criteria for IED.

Future aspect of IED

Even though it might be challenging to forecast the course of any mental health issue, there are some probable developments for IED in the future. Better Diagnosis and Treatment acknowledges and understands the IED grow, there might be more effective instruments for identifying the problem. Additionally, more potent therapies like psychotherapy and medication might be created.

Early Detection and Prevention of IED research is successful in identifying IED risk factors, the disorder may be more easily identified and treated before its symptoms worsen. To assist people in developing good coping mechanisms and avoiding aggressive behaviour, prevention programmes could be created. Co-Occurring Disorders frequently co-occurs with other mental health diseases like substance use disorders, depression, and anxiety. The treatment of people with numerous illnesses may be better integrated in the future, which would improve IED patients' results.

Reducing Social Stigma and discrimination associated with mental health issues can keep people from getting the treatment they need. It's likely that people with IED will feel more at ease seeking support and treatment as society attitudes continue to change. Research Advances progresses, new knowledge about the disorder's fundamental causes, potential genetic or molecular indicators, and more efficient therapies may become available. This might result in substantial advancements in the diagnosis and treatment of the illness.

Case study

A 31-year-old man came in with the characteristics of being distant, depressed, harbouring strong guilt feelings, and considering harming himself. When his wife discovered that he was having an extramarital affair with a well-known relative, the symptoms slowly started to appear. His emotions of depression worsened as a result of his wife's departure, and he began to consider suicide. He had an accident and began to bleed heavily while riding his motorbike late at night. He enjoyed the taste and fragrance of his own blood as he tasted it. As a result, he began to slash his wrist frequently so he could suck his own blood. Additionally, the guy would chew the glass fragments, enjoying the pain the glass produced to his cheek and lips. He even resorted to head beating in an attempt to increase the amount of blood flowing from his scalp injuries. He was admitted to the mental hospital after his peculiar behaviour was noticed. He was admitted to the hospital and continued to exhibit symptoms. He was known to act distant and calm before erupting occasionally in fits of rage and hostility. He abused other patients and took joy in doing so. The incident lasted between 15 and 30 minutes before ending naturally. The person would recall the incident but would not provide a logical justification for his violent actions. He denied having experienced convulsions, head trauma, or amnesia. Nothing in the past suggested a history of psychoses. He denied harbouring any guilt complexes over his violent behaviour and denying a prior history of comparable incidents. He acknowledged that he occasionally drank alcohol but disputed that doing so was a contributing factor to his violent outbursts. His violent protests during the student election campaign and even stabbing an opposition leader were made clear by his thorough premonitory history. He was a disobedient student. He was also expelled from school for a while. In college, he had one failed relationship. Comprehensive medical analysis and central nervous system analysis were unremarkable. Each

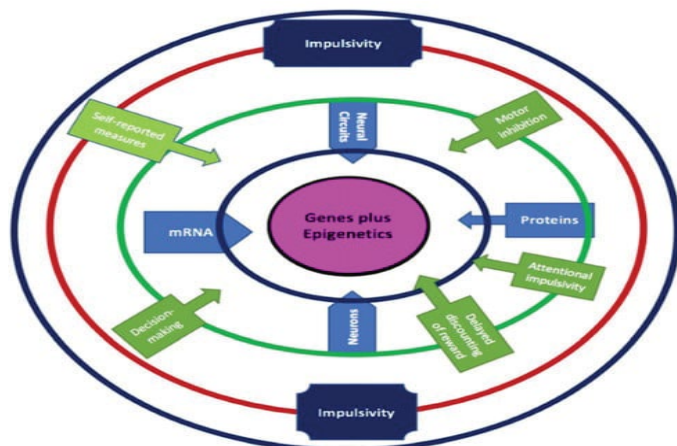


Figure 1. Different factors of IED.

haematological and biochemical parameter fell within the range of normal. Both the Electroencephalogram (EEG) and the Computed Tomography (CT) scan were normal. A mental health examination found that he was despondent. He then eventually joined the counselling and it proved to be helpful. The person was still asymptomatic after six months of monitoring, and there were no instances of unprovoked hostility or episodic outbursts. There was no proof of overt depressive thoughts. As may be observed in this instance, the symptoms stood out against a background of presumed stress. Due to the condition's rarity and the even more unusual way in which this person presented themselves, the case was all the more intriguing. After eliminating out biological factors and other psychogenic diagnoses, the diagnosis is always made. Thus, a thorough physical examination, a detailed medical history, and repeated assessments of mental state made up the diagnostic process. It is also important to highlight that not all people with intermittent explosive disorder have a good outlook on life. The patient will frequently have a secondary mental illness or will be undergoing therapy in a non psychiatric setting, which will result in chronicity in these circumstances. In such cases patient remain undiagnosed and end up in the hands of law untreated.

Treatment

Medication and counselling are frequently used in conjunction to treat IED. Cognitive-behavioral therapy can teach the person to recognise the causes for their outbursts and create coping mechanisms to control their anger, while medications like mood stabilisers and antidepressants may assist to regulate the person's emotions. To protect the person and those around them, hospitalisation may be required in extreme circumstances. People with IED should get professional care as soon as possible since untreated symptoms can seriously damage their personal and professional lives and endanger both themselves and other people.

Discussion

As may be observed in this instance, the symptoms stood out against a background of presumed stress. Due to the condition's rarity and the even more unusual way in which this person presented themselves, the case was all the more intriguing. After eliminating out biological factors and other psychogenic diagnoses, the diagnosis is always made. Thus, a thorough physical examination, a detailed medical history, and repeated assessments of mental state made up the diagnostic process. It is also important to highlight that not all people with intermittent explosive disorder have a good outlook on life. The patient will frequently have a secondary mental illness or will be undergoing therapy in a non psychiatric setting, which will result in chronicity in these circumstances.

Conclusion

Multiple data sets used in research that support the validity of intermittent

explosive disorder consistently demonstrate that, however it is defined, it is a disorder that is widely prevalent across studies and countries, has significant neurobiological findings, and is known to be responsive to treatment. These findings imply that intermittent explosive disorder has strong diagnostic validity, which is required for DSM-5 recognition and inclusion.

Conflict of Interest

The authors state no conflict of interest.

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