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The Role of Molecular Aspects in the Occurrence of Febrile Seizures

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A B S T R A C T

Febrile seizures are the result of complex interactions between multiple molecular components in the child's central nervous system, including changes in neurotransmitters, neuronal activity, and the brain's inflammatory response. When a child has a fever, there is an increase in body temperature, which triggers a series of molecular changes in the brain, affecting electrical signaling pathways and triggering characteristic seizures. The literature search process was carried out on various databases (PubMed, Web of Sciences, EMBASE, Cochrane Libraries, and Google Scholar) regarding studies of molecular aspects of febrile seizures. This study follows the preferred reporting items for systematic reviews and meta-analysis (PRISMA) recommendations. An increase in body temperature (fever) is the main trigger for febrile seizures. Fever can result in changes in brain chemistry, including changes in neurotransmitters and inflammatory responses, which can affect the molecular pathways that trigger seizures. Glutamate is the main neurotransmitter that plays a role in triggering seizures. Increased glutamate release during fever can trigger excessive activity in neurons. On the other hand, GABA, a neurotransmitter that plays a role in dampening neuronal activity, may also be involved, and an imbalance between glutamate and GABA may occur during seizures. Genetic factors play a role in susceptibility to febrile seizures. Several genes, such as SCN1A and GABRG2, have been identified as potentially increasing the risk of febrile seizures, especially those of a complex nature. Febrile seizures usually do not cause permanent changes in brain structure. However, in some very rare cases, such as EASIFE, temporary changes in brain structure may occur.

1. Introduction

Febrile seizures are a common neurological condition that occurs in childhood, often in response to a rise in body temperature caused by fever. Although febrile seizures themselves are usually temporary and rarely have a long-term impact on a child's development, understanding the molecular aspects in the pathophysiology of febrile seizures has an important role in unraveling the mystery behind this phenomenon. Febrile seizures are the result of complex interactions between multiple molecular components in the child's central nervous system, including changes in neurotransmitters, neuronal activity, and the brain's inflammatory response. When a child has a fever, there is an increase in body temperature which triggers a series of molecular changes in the brain, affecting electrical signaling pathways, and triggering characteristic seizures. Over the past decades, intensive research has helped to reveal several molecular aspects involved in the pathophysiology of febrile seizures.[1,2]

An increase in body temperature (fever) is the main trigger factor for febrile seizures. Fever can result in chemical changes in the brain, including changes in neurotransmitters and inflammatory responses. The brain inflammation associated with fever may affect the molecular pathways that trigger seizures. An increase in body temperature can affect the electrolyte balance in the brain. Increased neuronal activity and release of neurotransmitters such as glutamate may

occur, and this may affect electrical conductivity in the brain. Glutamate is the main neurotransmitter involved in seizures. Increased glutamate release during fever can trigger excessive activity in neurons. GABA (gamma-aminobutyric acid), a neurotransmitter that plays a role in dampening neuronal activity, may also be involved. During seizures, the balance between glutamate and GABA may be disturbed. Gamma-aminobutyrate (GABA) is a dampener system that is important in controlling neural activity. In febrile seizures, there is a disturbance in the GABA system, which can result in increased nervous activity. In some cases, febrile seizures can cause temporary changes in a child's brain structure. These changes may affect molecular pathways involved in brain function and seizures. Febrile seizures often occur in response to infections, and infections can affect the body's immune response. The immune response to infection also has molecular aspects involved in the pathophysiology of febrile seizures.[3,4]

2. Methods

The literature search process was carried out on various databases (PubMed, Web of Sciences, EMBASE, Cochrane Libraries, and Google Scholar) regarding the study of molecular aspects of febrile seizures. The search was performed using the terms: (1) "febrile seizures" OR "febris" OR "infection" OR "pathophysiology" AND (2) "febrile seizures" OR "molecular." The literature is limited to clinical studies and published in English. The literature selection criteria are articles published in the form of original articles about the study of molecular aspects of febrile seizures, studies were conducted in a timeframe from 2013-2023, and the main outcome of the study of molecular aspects of febrile seizures. Meanwhile, the exclusion criteria were studies that were not related to the study of molecular aspects of febrile seizures, the absence of a control group, and duplication of publications. This study follows the preferred reporting items for systematic reviews and meta-analysis (PRISMA) recommendations.

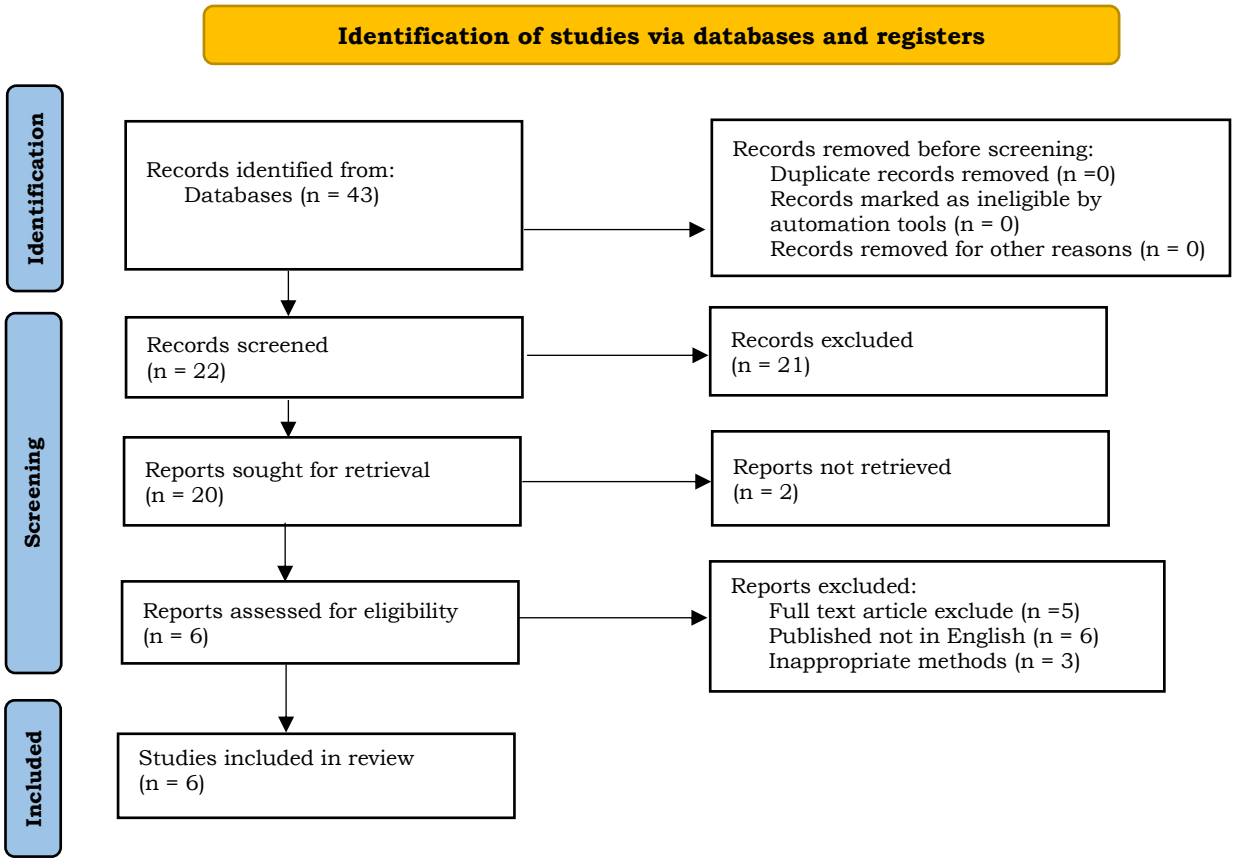

Figure 1. PRISMA flowchart.

3. Results and Discussion

The role of temperature and inflammation

Febrile seizures usually occur in response to fever, which is often caused by an infection such as a viral or bacterial infection. This increase in body temperature can trigger seizures in susceptible children. Rapidly rising body temperature can affect brain function and stimulate nerve pathways that trigger seizures. An increase in body temperature can affect chemistry in the brain. During fever, changes occur in the concentration of chemicals such as neurotransmitters. For example, high body temperature can affect the metabolism of neurotransmitters such as glutamate and GABA, which have an important role in regulating neural activity. Fever is often a sign of inflammation in the body, which is a natural response to infection. This inflammation can also include the brain, known as encephalitis. Brain inflammation can affect molecular pathways in the brain, trigger the release of inflammatory chemicals, and disrupt neuronal activity. Inflammation and changes in neurotransmitter balance can disrupt the molecular pathways that trigger seizures. Excessive activity in neurons, accompanied by uncontrolled release of neurotransmitters, can cause a child's body muscles to contract and relax rapidly, creating seizure symptoms.[5-7]

Electrolyte balance

When body temperature rises due to fever, this can affect the electrolyte balance in the brain. Electrolytes, such as sodium, potassium and chloride, are ions that are important in maintaining electrical conductivity in the brain. Increased body temperature can cause changes in electrolyte distribution, which in turn can affect neuronal function. Increasing body temperature can also increase neuronal activity in the brain. Increased neuronal activity can cause the release of more neurotransmitters, including glutamate, which is the main neurotransmitter in the brain that plays a role in transmitting electrical signals between neurons. Changes in the release of neurotransmitters, particularly glutamate, can affect electrical conductivity between neurons in the brain. Increased glutamate can trigger excessive activity in neurons, which in turn can trigger seizures. Seizures are the result of uncontrolled electrical activity in the brain.[8-11]

Role of neurotransmitters

Glutamate is the main neurotransmitter that plays a role in stimulating neuronal activity. During fever, glutamate release can increase significantly. Increased glutamate can trigger excessive activity in neurons, resulting in an uncontrolled cascade of electrical signals. This can cause the body's muscles to contract and respond with spasm symptoms. GABA (gamma-aminobutyric acid) is a neurotransmitter that plays a role in reducing neuronal activity. Its function is to inhibit or control the excessive response of neurons to stimuli. During febrile seizures, the balance between glutamate and GABA may be disturbed. Decreased GABA response and increased glutamate may make neurons more susceptible to hyperactivity, which is one of the mechanisms underlying seizures. It is important to remember that the balance between glutamate and GABA is critical for healthy brain function. In the situation of febrile seizures, this imbalance occurs temporarily and contributes to the development of seizures. This is why the development of therapies aimed at regulating the balance between these neurotransmitters could be a potential approach in the treatment of febrile seizures.[12-14]

Genetic

Genetic factors play an important role in a person's susceptibility to febrile seizures, and several genes associated with this condition have been identified. Mutations in certain genes can increase the risk of febrile seizures, especially complex febrile seizures which tend to be more serious. SCN1A Gene: Mutations in the SCN1A gene are associated with the risk of complex febrile seizures, including Dravet syndrome, which is a more serious form of febrile seizures. The SCN1A gene encodes the Nav1.1 subunit in a voltage-gated sodium channel that is involved in the regulation of neuronal activity. Mutations in this gene can disrupt the function of these sodium

channels and increase the tendency to seizures. GABRG2 Gene: The GABRG2 gene encodes a GABA-A receptor subunit, which is an important component in the central nervous inhibitory system. Mutations in this gene can affect GABA receptor function and the balance between excitation and inhibition in the brain. It may also contribute to susceptibility to seizures. Apart from SCN1A and GABRG2, there are many other genes that also play a role in susceptibility to febrile seizures. Genetic research has helped understand the role of genetics in this condition and may aid in the identification of individuals at high risk.[15-17]

Changes in brain structure

Febrile seizures in children are usually temporary and rarely cause significant structural changes in the brain. Nevertheless, in very rare cases, some temporary changes in brain structure may occur due to repeated or prolonged febrile seizures. This is known as "encephalopathy associated with status epilepticus in febrile infection-related epilepsy syndrome" (EASIFE). EASIFE is a very rare condition and involves structural changes in the brain as well as changes in the molecular pathways involved in brain function. However, EASIFE is different from regular febrile seizures, and the majority of children who experience febrile seizures do not experience significant structural brain changes. Febrile seizures that occur in most children do not cause permanent changes in brain structure. However, it is important to understand that any seizures that last a long time or recur within a short period of time should be immediately evaluated and given medical treatment. Prolonged seizures can have serious consequences and require appropriate treatment. Changes in brain molecular pathways during febrile seizures are generally temporary, and the child's brain usually recovers after the seizure. However, further understanding of the mechanisms involved in these transient changes may aid in the development of better treatment strategies and may aid in the identification of children at high risk for recurrent febrile seizures.[18-20]

4. Conclusion

Febrile seizures are a neurological condition that commonly occurs in children in response to a rise in body temperature caused by fever. Molecular aspects play an important role in the pathophysiology of febrile seizures, and a deeper understanding of these may help in more effective treatment and prevention. An increase in body temperature (fever) is the main trigger for febrile seizures. Fever can result in changes in brain chemistry, including changes in neurotransmitters and inflammatory responses, which can affect the molecular pathways that trigger seizures. Glutamate is the main neurotransmitter that plays a role in triggering seizures. Increased glutamate release during fever can trigger excessive activity in neurons. On the other hand, GABA, a neurotransmitter that plays a role in dampening neuronal activity, may also be involved, and an imbalance between glutamate and GABA may occur during seizures. Genetic factors play a role in susceptibility to febrile seizures. Several genes, such as SCN1A and GABRG2, have been identified as potentially increasing the risk of febrile seizures, especially those of a complex nature. Febrile seizures usually do not cause permanent changes in brain structure. However, in some very rare cases, such as EASIFE, temporary changes in brain structure may occur.

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