


Opinion

# Untreated Early Childhood Caries and Possible Links with Brain Development

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**Abstract:** Untreated early childhood caries (ECC) is a global public health concern. In the short term, untreated ECC can lead to pain, infection, and disrupted sleep, among other issues. In the long term, it is associated with poor oral health in later life, increased risk of caries in permanent teeth, and adverse effects on physical and psychological development. There may be a link between untreated ECC and adverse cognitive and neurodevelopmental outcomes in young children, although the exact pathways are not fully understood. One possible pathway is through the relationship between mastication and brain stimulation. Impaired masticatory function due to ECC can affect the hippocampus, a key region responsible for memory and learning. Furthermore, untreated ECC can cause chronic inflammation, leading to the release of pro-inflammatory cytokines that may damage the brain. Sleep disturbances resulting from ECC-related pain and discomfort can also impact brain development and cognitive functioning. Additionally, frequent use of antibiotics and analgesics to address ECC-related infections can disrupt the gut microbiome, potentially affecting the brain through the gut–brain axis. Untreated ECC can cause nutritional deficiencies and elevated nutritional risk, and can further hinder brain development. Addressing ECC comprehensively with early childhood health initiatives can help mitigate potential long-term consequences and promote optimal brain development in young children.

**Keywords:** dental caries; children; preschooler; cognitive function; nutrition; inflammation; microbiome



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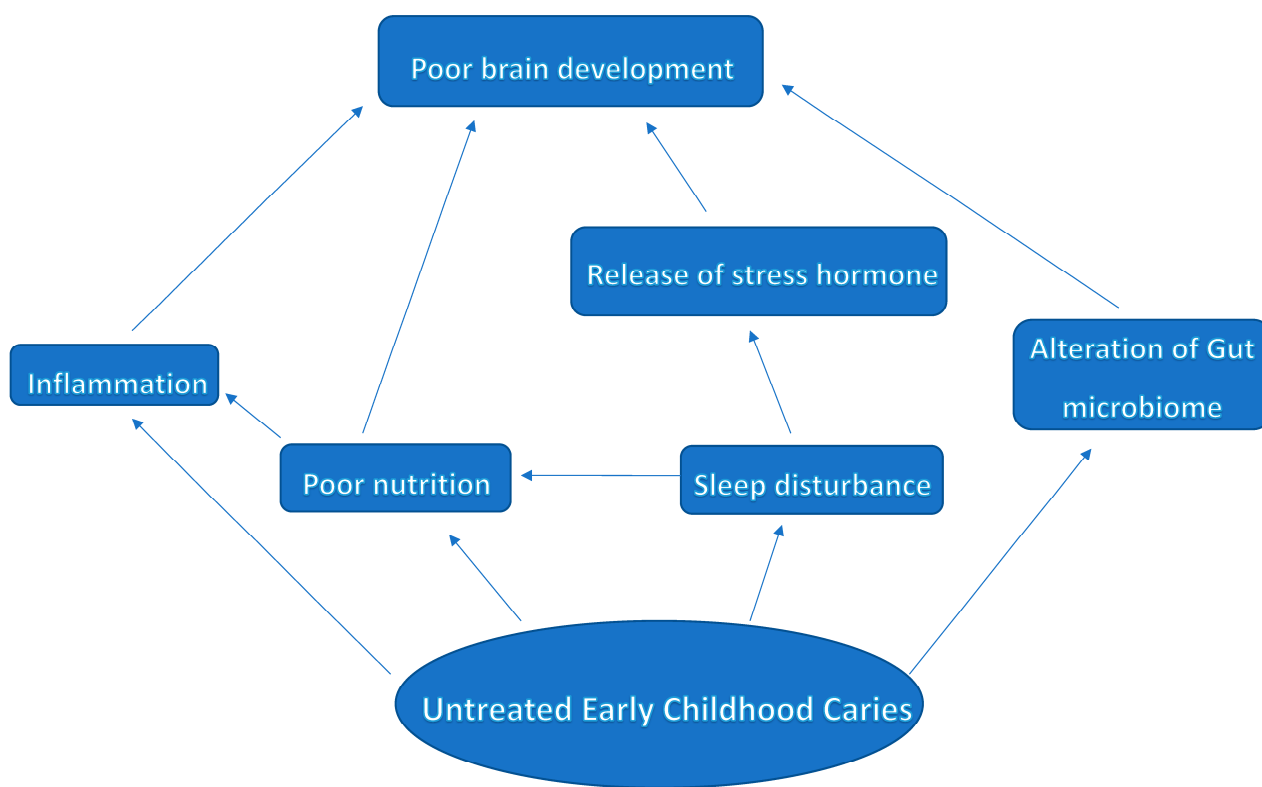


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## 1. Introduction

Early childhood caries (ECC) is a prevalent oral health condition that affects children worldwide [1]. ECC is characterized by the presence of dental caries in primary teeth [2]. This condition has significant implications for children’s physical, mental, and social well-being. In the short term, untreated ECC results in pain, infection, poor appetite, disturbed sleep, hospitalization, loss of school days, reduced ability to learn, poor concentration, and eventual premature loss of the tooth [3], which causes poor mastication [4]. In the long term, untreated ECC is linked to poor oral health in later life, high risk for caries in the permanent dentition, poor physical growth and development, poor psychological development, and poor quality of life [3,5]. Although ECC has long been recognized as a major public health concern, recent research has highlighted potential links between untreated ECC and adverse cognitive and neurodevelopmental outcomes in young children [6–10]. This is because ECC occurs in the first few years of life when the brain is undergoing rapid and sensitive development of its neural systems. The exact pathways connecting ECC to poor brain

development are not yet fully understood. However, the conceptualization of the pathway is represented in Figure 1.



**Figure 1.** Conceptual framework of the pathways associating untreated early childhood caries with poor brain development.

### 1.1. Mastication and Brain Development

One possible pathway is the relationship between masticatory force and brain stimulation. Animal and human studies have suggested a potential causal link between mastication and cognitive function [11,12]. Mastication plays a role in maintaining cognitive functions in the hippocampus by providing peripheral sensory input, which supports and enhances cognitive function [13]. The hippocampus is the central component of a large neural network involved in memory processes, especially spatial memory and learning in the central nervous system [14]. Neurons in the hippocampus connect to neural circuits controlling cognition, memory, and motor functions. A huge percentage of brain development occurs postnatally, a period characterized by the formation of masticatory habits. Therefore, impaired masticatory function can lead to morphological and functional changes in the hippocampus, resulting in deficits in hippocampus-dependent spatial memory [15,16].

Unfortunately, untreated ECC can cause pain, which leads to avoidance of using the affected tooth, resulting in a reduction in masticatory force [3,4]. Moreover, the presence of untreated ECC can lead to tooth loss, further impairing masticatory function [17]. The loss of teeth has been associated with specific changes in grey matter volume in various brain regions. These changes include an increase in grey matter volume in regions responsible for the fear response, learning, memory consolidation, and the trigeminal spinal tract nucleus. Conversely, there is a decrease in grey matter volume in regions controlling movement, motor processing/control, emotions, working memory, problem-solving behavior, and the trigeminal motor nucleus [18].

One of the possible earliest signs of the impact of tooth loss on the brain is the resultant speech disorder due to the modification of occlusal forces [19]. Tooth loss, especially in the anterior region of the oral cavity, can lead to speech distortion and difficulties in pronouncing certain sounds, known as “labial” or “dental” sounds, that involve the lips as

active articulators [20]. These “labial”, “bilabial”, and “labio-dental” sounds are produced when the tongue interacts with or comes close to the upper and/or lower anterior teeth in a coordinated action with the tongue [21]. Additionally, there are various other types of speech sounds related to the position and involvement of the teeth and tongue. These include interdental sounds, where the teeth act as passive articulators; alveolar sounds, produced just behind the teeth by placing the tip of the tongue against the alveolar ridge; palatal sounds, formed when the tongue approaches the hard palate; velar sounds, created when the back of the tongue contacts the soft palate or velum; and glottal sounds, produced in the region of the glottis. These different types of sounds contribute to the complexity and diversity of human speech [22] that are developed early in life.

The process of producing these sounds involves intricate neural connections that coordinate the interactions between the brain and various oral structures, such as the teeth, tongue, muscles of mastication, lips, and vocal cords [23]. These neural pathways develop and strengthen during childhood and adolescence, a critical period when language skills are rapidly evolving [24]. When tooth loss occurs during this crucial phase of brain development, the neural connections involved in speech production may face challenges [25]. Consequently, children with missing teeth may experience difficulties in articulating speech clearly and fluently [26]. In response, the brain may undergo adaptation and reorganization of its neural pathways to compensate for the altered oral structure and the resulting speech disorders [27]. This happens because tooth loss causes the modifications of neuronal activity that can lead to alterations in neurotransmission and synaptic strength known as synaptic plasticity [28]. The phenomenon brings about adjustments in intracortical microcircuitry, thereby impacting the organization of cortical maps and cytoarchitecture. These changes serve as the foundation for long-term modifications in motor performance [29].

### *1.2. Inflammation and Brain Development*

Untreated ECC leads to infection and chronic inflammation resulting in elevated levels of pro-inflammatory cytokines and a resultant arithmetic progression with the severity of ECC [30]. The pro-inflammatory cytokines produce free radicals that generate peroxides, Prostaglandin E2, interleukin 6, tumor necrotizing factor-alpha, and cysteinyl leukotrienes that are powerful agents in the inflammatory response [31–33]. Infection and agents of inflammation can damage the brain and ECC may cause the dissemination of bacteria from distant sources with associated damage to the white brain matter [34,35] whose maturation is associated with the development of cognitive functions in early childhood [36]. The released endotoxins can initiate a brain-damaging process, and the inflammatory proteins released play a role in mediating the damage [37,38]. A corollary potential is that maternal untreated caries may be a risk factor for chorioamnionitis, a risk factor for intrapartum brain damage [39–41], which is also associated with host dental caries microbacteria [42].

In addition, pain associated with untreated ECC can contribute to elevated levels of stress, which may have a negative impact on brain development. Prolonged exposure to stress hormones, such as cortisol, activates the hypothalamic–pituitary–adrenal axis [43]. Cortisol can disrupt the delicate balance of neurochemicals in the brain and hinder the growth of neural connections necessary for optimal cognitive functioning [44,45]. The effect is a decrease in memory and cognitive flexibility, which is reversible in a healthy resilient brain [46]. Specifically, cortisol impairs the process of memory retrieval in a non-linear fashion [47,48] and it affects the working memory [49].

Moreover, untreated ECC can result in chronic systemic inflammation, leading to disruptions in the functional connectivity within the parieto-occipital lobe [50]. This chronic inflammation causes structural remodeling in brain regions crucial for achieving developmental milestones [50]. During early years of life, oligodendrocyte progenitor cells undergo proliferation and differentiation, contributing to the development of astrocytes and oligodendrocytes. This process plays a vital role in establishing neuronal connections, ensuring proper neural signaling [51]. Additionally, myelination processes continue in early childhood, but chronic inflammatory processes can disrupt these processes, affecting

the number of synapses and the integrity of the myelin sheath [50]. Consequently, ECC-induced chronic inflammation can lead to issues such as poor memory, impaired functional connectivity within the brain, and adverse cognitive functions.

### 1.3. Sleep Disturbances and Brain Development

Untreated dental caries can cause sleep deprivation [3]. The pain and discomfort resulting from untreated ECC can additionally disturb sleep patterns [52]. Sleep plays a vital role in the development of the brain and cognitive functioning [52]. Disrupted sleep can hinder the consolidation of memories, impede attention and concentration, and impair overall cognitive development [53,54]. Moreover, poor sleep quality may contribute to behavioral issues and impact a child's emotional well-being, potentially affecting their social and cognitive growth [55]. Furthermore, sleep deprivation in children triggers the release of stress hormones [56]. Conversely, sleep disturbances can predispose children to the development of ECC; thus, the relationship between sleep disturbances and ECC can be described as bidirectional. Irregular sleep patterns, inadequate sleep duration, and going to bed late have been linked to decreased self-regulation of appetite, potentially leading to late-night eating habits [57–59], which can contribute to the risk of ECC through increased intake of a sugary diet at bedtime (although increased intake of sugar before bedtime causes a delay in sleeping [60]) [61] or indirectly through obesity [62]. In addition, inadequate sleep alters the immune status and may predispose children to carious activity via *Streptococcus mutans* [63]. Untreated ECC can also lead to sleep disturbances which can in turn affect cortisol production [64].

### 1.4. Gut Microbiome and Brain Development

Moreover, the frequent administration of antibiotics and analgesics to address infections and pain related to untreated ECC can disrupt the balance of the gut microbiome [65]. The gut microbiome plays a vital role in the development and functioning of the brain, and emerging research indicates that diverse gut microbiota can have either a positive or a negative influence on cognitive processes and mental well-being [66].

The brain–gut axis forms a complex, two-way communication network linking the enteric and central nervous systems [67]. Through this connection, sensory signals from the gut are transmitted to the central nervous system via the Vagus nerve, influencing reflexes and impacting mood, cognition, and mental well-being. At the same time, the brain sends signals that regulate gut anatomy and physiology. This bidirectional communication allows the gut–brain axis to monitor and integrate gut functions while establishing connections between the emotional and cognitive centers of the brain. Additionally, gut bacteria have the capability to produce and release neurotransmitters that can communicate with and affect the central nervous system via the Vagus nerve [68,69]. The gut microbiome is sensitive to various factors, including stress and medication usage [70], which can lead to an imbalance known as dysbiosis [71,72]. Dysbiosis triggers an increase in the secretion of pro-inflammatory cytokines, which can have a detrimental impact on the brain [73,74].

### 1.5. Nutritional Implications

Untreated ECC leads to the generation of pro-inflammatory cytokines, which are strongly linked to an elevated nutritional risk [75] and can hinder brain development [76]. Severe ECC is also connected to challenges in eating, decreased food consumption, and deficiencies in iron, vitamin A, vitamin D, and albumin [77–80]. These nutritional deficiencies can potentially impede brain development and compromise cognitive capabilities [81–83], as the developing brain relies on adequate nutrition, especially protein deficiencies, which facilitate its growth, optimal functioning, and plasticity [84,85].

## 2. Discussion

Early childhood caries is a preventable condition; however, regrettably, it continues to be highly prevalent among children [4]. Moreover, the risk of ECC is disproportionately

higher among individuals with a low socio-economic status [86], who often face various challenges that can negatively impact their brain health. Children from low socio-economic backgrounds are more likely to exhibit brain maturation patterns characterized by lower volume and slower rates of change as they develop [87]. This review suggests that untreated ECC may compound the risk for poor brain development in children with a low socio-economic status.

Early intervention and preventive strategies are crucial in mitigating the potential impact of untreated ECC on brain development. Promoting good oral hygiene practices, such as regular toothbrushing with fluoride toothpaste, along with limiting sugary foods and beverages, are essential preventive measures. Regular dental check-ups from an early age can facilitate early detection and prompt treatment of ECC, reducing the risk of complications. Country-level policies and regulations with advocacy for the addition of dental treatment into the National Health Insurance Scheme to assist children from the low socio-economic class to have access ECC treatment, and an active drive to monitor these regulations, can facilitate improved ECC management and control.

Currently, many oral healthcare programs targeting children are school-based. However, it is ironic that a significant number of pre-school children, who are at risk of developing ECC, are not part of formal school systems [88]. As a result, they are unable to benefit from these school-based interventions. Nevertheless, there is evidence suggesting that health promotion efforts among pre-school children can have a lasting impact on their health behaviors [89], and there are models available for integrating health promotion programs for this age group [90,91]. Despite this, the process of generating and scaling up evidence to drive the implementation of ECC prevention programs has been exceedingly slow. What is lacking is the political willpower to drive the change.

In addition, it is crucial to foster collaboration between oral health professionals, neurodevelopmental pediatricians, and early childhood educators. Such collaboration can increase awareness about the significance of oral health in overall development, enable the implementation of preventive strategies, and provide appropriate care for children affected by ECC. It is also important to incorporate oral health into programs and interventions for early childhood development at national and international levels. Educating parents and caregivers about proper oral hygiene practices, the importance of a balanced diet, and the potential consequences of untreated ECC can empower them to take proactive comprehensive and holistic measures to safeguard their children's oral health and support their brain development.

This opinion piece has its limitations. We acknowledge that this was a consensus review that drew on our expert knowledge of the subject matter, and the evaluation of research to reach our collective conclusions. However, the main weakness lies in the potential for bias during article selection as we may have selected articles that confirm our own views and, thereby, unintentionally introduced bias. The information aligns better with the specifics of the focus of our discussion, and potentially offers more relevant guidance for further work on the topic of interest. There are no established standards or guidelines governing the process of generating articles for an opinion piece and thus we share some insights into the issue of understanding that our thorough grasp of the overall state of the science concerning the problem is limited and further studies are needed. The group will build on the conceptual framework from this study to inform our future studies.

### 3. Conclusions

Untreated ECC may have plausible links with disturbances in brain development, highlighting the need for early intervention and preventive measures. The chronic inflammation, pain, nutritional implications, and sleep disruptions associated with untreated ECC can adversely affect neurodevelopmental outcomes in young children. Recognizing the connections between untreated ECC and disturbances in brain development underscores the importance of a comprehensive approach that integrates oral health care within early childhood health and development initiatives. By prioritizing oral health for pre-school

children and implementing timely interventions, we can strive to mitigate the potential long-term consequences of untreated ECC and promote optimal brain development in young children.

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