


Chapter 12

Neurocognitive Sequelae in Children With Diabetes Mellitus: A Narrative Review of the Effects and Directions for Future Research

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ABSTRACT

In recent times, diabetes mellitus (DM) has evolved from being viewed mainly as a medical issue linked to metabolic disturbances to a multifaceted condition that carries potential implications extending well beyond the management of blood sugar levels. However, an area that hasn't been examined extensively is its impact on the neurocognitive functions. Various illness-related risk factors are associated with neurocognitive deficits among children with type 1 diabetes. Considering the essential function that influence diabetes-related outcomes and the overall quality of life, it is crucial to incorporate psychological support as a standard component of diabetes care. The current narrative review aims to carefully analyze the existing body of research concerning the potential influence of diabetes on the fluctuations in neurocognitive functioning during the period from infancy to adolescence, identify the pertinent clinical implications and treatment strategies and interventions, and highlight the areas in the literature, which require further exploration and comprehension.

INTRODUCTION

Chronic diseases, such as ***Diabetes Mellitus (DM)***, can impair the neurodevelopment and cognitive function, resulting in disruptions in employment and mental health from childhood into adulthood, as the neural development persists from the early embryonic stages through adolescence (Ibrahim et al., 2023). Cellular nerve development, transformation, and synaptogenesis occur in life with significant

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activity during the prenatal phase and the early years of childhood (Stanislawska-Kubiak et al., 2024). *Type 1 diabetes (T1D)* is a serious and persistent illness, characterized by the lack of insulin, which plays a crucial role in glucose metabolism, which can result in deficits within the brain, potentially impacting cognitive function (Naguib et al., 2009).

A substantial body of research has shown that diabetes, along with its microvascular complications and control through insulin and other medications, can lead to mild to moderately severe neurocognitive dysfunctions because of the structural and functional alterations within the central nervous system (Ryan et al., 2016), involving myelination and the establishment of synaptic networks. The administration of insulin, whether through multiple daily injections or constant infusion through an insulin pump, represents a partial remedy for the inherent deficiency in the body's natural insulin production. The non-physiological nature of this treatment leaves patients susceptible to fluctuations in blood glucose levels, experiencing episodes of hypo- and hyperglycemia throughout their whole lives (Cato & Hershey, 2016).

Prior to the establishment of a clinical diagnosis and the initiation of insulin therapy, kids diagnosed with type 1 diabetes may endure extended periods of severe hyperglycemia. At the diagnosis onset, in thirty percent of the patients, sustained hyperglycemia can result in a serious metabolic imbalance, known as *diabetic ketoacidosis (DKA)*, which may result in brain swelling and decreased cerebral blood flow, which could influence the ongoing neural development, although this is not invariably the case (Cato & Hershey, 2016). In general, the likelihood of going through such issues tends to be greater during childhood and adolescence than throughout the other life stages.

On the one hand, chronic hyperglycemia can also result in adverse effects that can impact various organs, including the retina, the heart, the kidneys, the peripheral nerves, and the brain, among people of all ages. In addition, the immature nervous system of young children is particularly susceptible, on the other hand, to hypoglycemic events, as well, and the adrenergic response during this period is less developed. The regular experiences of hypoglycemia could result in various neurological impairments. The possible cognitive effects of severe hypoglycemia, including the risk of coma, represent a significant concern for clinicians, patients, and their families.

During this stage, maintaining proper glucose control is essential, as it significantly influences the development of the central nervous system. Consistent fluctuations in the glycemic levels may result in lasting impairments in neurocognitive functioning (Tau & Peterson, 2010). An earlier onset of T1D and longer duration are widely acknowledged as significant risk factors for cognitive impairment (Biessels & Whitmer, 2019), which encompass diminished overall mental performance and specific deficits in tasks evaluating visuospatial and executive functions (Bjorgaas et al., 1997; Lin et al., 2010), attention, learning and memory (Gaudieri et al., 2008; Lin et al., 2010; Zilliox et al., 2016), and information processing speed (Lin et al., 2010; Northam et al., 2009; Ryan et al., 1985). Children who receive a diagnosis in early childhood, particularly prior to the age of 5, tend to exhibit less favorable outcomes regarding their academic performance, motor skills, and hand coordination (Stanislawska-Kubiak et al., 2024; Litmanovitch et al., 2015). The current narrative review aims to carefully analyze the existing body of research concerning the potential influence of diabetes mellitus on the fluctuations in neurocognitive functioning during childhood, and more specifically *the period from infancy to adolescence*, identify the pertinent clinical implications and treatment strategies and interventions, as well as highlight the areas in the literature which require a more thorough exploration and comprehension. No further limitations were imposed regarding the type of surveys utilized throughout this review.

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