Type I Diabetes Mellitus

Subjects: Clinical Neurology

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Definition

A considerable endeavor had taken place in order to understand the associated challenges for children and adolescents with Specific Learning Disorder (SLD) and Type 1 Diabetes Mellitus (T1DM) but also in order to describe the necessary skills and approaches that the care givers have to develop to assist both children and parents.

1. Introduction

School performance, especially in children with specific learning disorders (SLD), is adversely affected by the coexistence of a chronic disease, such as Type 1 Diabetes Mellitus (T1DM) (previously called juvenile diabetes or insulin-dependent diabetes). Being diagnosed with a chronic illness can be overwhelming; especially at the start it can be stressful for the child and its family. We are conscious that living with T1DM can be really challenging for children, adolescents, and their families, regarding the complexity of the treatment, the involvement of the adult care givers and the needed support from the school setting. Children with T1DM and SLD confront major challenges, managing both insulin and learning difficulties within the school setting.

Data from studies reviewed in this research, show that students with learning difficulties have higher rates of diabetes compared to the general population. The report of Public Health England, NHS Digital in 2016, supports the occurrence of higher rates of both diabetes types, in all age groups, in the population with SLD compared to the general population, and with early onset, recorded at a younger age [1][2]. In addition, a greater risk of autoimmune manifestations-including T1DM-that is recorded in Down's syndrome [3], could explain the T1DM leading rates among children and adolescents with SLD [2]. Furthermore, SLD is also associated with higher rates of developing Type 2 Diabetes Mellitus (T2DM) later in adulthood [4][5][6], higher risk of obesity, due to a lifestyle with low level of exercise and high-fat diets, as well as higher levels of prescribed antipsychotic medication [2][7].

Initially, since in literature we find only a few facts about the coexistence/comorbidity of SLD and T1DM, it is important to clarify some points about prevalence and phenomenology that characterize them.

1.1. Specific Learning Disorders (SLD)

Specific learning disorder (SLD) is also referred as learning disorder/disability, representing a neurodevelopmental [8] and neurobiological [9] disorder, that usually begins during the early school-age, and possibly not recognized until adolescence and even adulthood [8][10][11][12]. According to the diagnostic criteria of DSM-5, SLD is characterized by three types of continuous difficulties in the ability of learning, concerning one out of three fundamental domains of reading, writing and math; manifesting as a failure in the development of these skills, in correspondence to the expected for the age grade [8][9][13]. Apart from these three core areas, other disorders, such as memory problems, inattention and difficulties in social interaction, may also contribute fundamentally to failure in school performance, requiring a more specific intervention [13]. If not recognized and managed at an early age, beyond having lower academic achievement, ongoing difficulties may have a negative long-term impact in adult life [8][9][10][14]. Various difficulties, such as low self-esteem, behavioral and social problems, due to school failure, are associated with low academic achievements and dropping out of school in youths; mental distress, unemployment or under- employment later in adult life [8][10][11][15][16][17][18][19]. In numerous studies, SLD reflects different prevalence in relation to age, gender, psychosocial stage of development and environmental features [15]. The comorbidity of SLD with other disorders, is usually associated with more complicated manifestation and severe emotional and behavioral symptoms, that render interdisciplinary intervention crucial [15].

SLD is a multifactorial disorder, caused by inherent or acquired factors affecting brain structure and function[20]. Genetic and family load, developmental factors, cognitive skills, native language, academic degree, environmental factors, such

as socioeconomic status, are mentioned in many studies as severe etiological factors [13][15]. In Table 1 various risk factors are defined as predeterminants for SLD, indicating that the prevalence of SLD is increased among children with the mentioned characteristics regarding family history, medical history and socioeconomic status [13][15][21][22][23][24][25][26][27][28][29][30][31][32][33][34][35][36][37][38][39][40][41][42][43][44][45][46][47][48][49][50][51][52][53][54][55][56][57]. A plethora of research studies have indicated that the prevalence of SLD shows considerable cross-national variation [55] and gender variation, with higher rates among boys comparatively to girls [8].

Table 1. Risk factors for Specific learning disorder (SLD).

Family history
1. SLD [13][21][22][23][27][29][30][31]
2. Level of parental education [27][32]
3. Special education services or educational supports [27][28][32]
4. ADHD diagnosis [27][29][33]
5. Not reading for pleasure [27][34]
6. Genetic disorders [27][35]
Medical history
1. Prenatal and perinatal: premature labor or after risky pregnancies (diabetic gravidas), low/very low birth weight, complicated deliveries, hypoxia during labor and delivery, low Apgar score, neonatal jaundice, in utero substance exposure (e.g., alcohol, tobacco, radiation exposure, infections) [27][36][37][38][40]
2. Other developmental (e.g., early speech-language delay [27][43] and mental health conditions (e.g., ADHD, disruptive behavior disorders, autism, anxiety disorders, and depression) [13][27]
3. Neurocutaneous disorders (e.g., neurofibromatosis, Sturge- Weber syndrome, tuberous sclerosis complex) [27][35]
4. Neurologic conditions or insults (e.g., seizure disorders, Tourette syndrome, history of central nervous system infection or irradiation or traumatic brain injury [27][29][35][42]
5. Genetic disorders, syndromes or metabolic disorders, chromosomal disorders (e.g., fragile X syndrome, Turner syndrome, Klinefelter syndrome) [27][31][41][42]
6. Medical conditions (e.g., recurrent otitis media, asthma) [27][29]
7. Certain chronic medical conditions (e.g., T1DM, HIV infection) [13][27]
Socioeconomic status

1. low-income families/low socioeconomic status [13][24][25][26]
2. cultural considerations [27][37][44]
3. environmental disadvantage [27][37][44]
4. poverty [27][34]
5. under stimulating environments [13][24][25][26]
6. neglect, abuse, domestic violence or unsafe home environment (e.g., parental substance abuse)[27][44]
7. Adverse childhood experiences [27][45]
8. Lack of adequate instruction [27][46]

Information from references [13][21][22][23][24][25][26][27][28][29][30][31][32][33][34][35][36][37][38][39][40][41][42][43][44][45][46].

Table 2 shows the differential diagnosis of SLD, as there are conditions with high risk of learning issues in children and adolescents -that may not meet the diagnostic criteria of SLD- and if left untreated, may be confused with SLD [13][17][27][58][59].

Table 2. Differential Diagnosis for Specific learning disorder (SLD).

1. Developmental delays (global and specific) [8][13][17][27][29][38][58][59][60][61]
2. Genetic syndromes or metabolic disorders [8][13][17][27][31][41][42][58][59]
3. Hearing impairment [8][13][17][27][58][59][62]
4. Visual impairment [8][13][17][27][58][59][63]
5. In utero substance exposure [27][38][40]
6. Mild intellectual disability (formerly mental retardation) [8][13][17][27][36][58][59][60][61]
7. Psychiatric conditions, ADHD or emotional disturbance (e.g., depression or anxiety) [8][13][17][58][59]
8. Neurocutaneous disorders (e.g., neurofibromatosis, Sturge- Weber syndrome, tuberous sclerosis) [8][13][17][27][35][58][59]
9. Neurologic conditions or insults (e.g., seizure disorders, Tourette syndrome, history of central nervous system infection or irradiation or traumatic brain injury [8][13][17][27][29][35][42][58][59]
10. Seizure disorder (e.g., absence, partial, partial- complex) [27][29]
11. Genetic causes [8][13][17][21][22][23][24][25][26]
12. Parent/school expectations that are discordant with the student's abilities and interests [8][13][17][58][59]
13. Environmental factors (e.g., lack of opportunity, frequent school absences, poor teaching, and cultural factors, such as English as a second language) [8][13][17][58][59]
14. lead poisoning, medication side effects, substance abuse [8][13][17][58][59]
15. Sleep disorders [27][63]

Information from references [8][13][17][27][29][31][35][36][38][39][40][41][42][58][59][60][61][62][63][64].

The assessment of these conditions includes a series of essential examination, laboratory diagnostic tests, and supplemental appraisal, or more specialized testing and/or referral such as blood lead level, audiological and vision screening tests etc. Qualitative observations and/or the student's report card can often identify SLD, but to make a formal diagnosis, psychometric testing is needed (Wechsler Intelligence Scale for Children- WISC) [13][27].

The presence of SLD along with the conditions listed above is common[13]. Anxiety disorders [27][62], behavioral disorders [27][37][65][66], depressive disorders [27][29][62], motor delays/ disorders [27][65], neurodevelopmental disabilities (such as Attention Deficit Hyperactivity Disorder-ADHD) [27][37][62][65], speech-language delays/disorders [27][29][30][39][43][60], social-emotional problems and substance abuse [27][67] are the most common comorbidities with SLD[27].

Regarding terminology, in the present literature review, the terms: "SLD", "Specific Learning Disability", "learning disability", "learning difficulties" [8][11][12][68]; refer to miscellaneous group of disorders/difficulties revealed through unsuccessful attempts to obtain knowledge, which subsequently could be retrieved and utilized efficiently [13]. The "SLD", which as a medical term, constitutes a diagnostic terminology [8], usually mentioned as "learning disorder" [8][11][12][68]; and the "Learning disability", as an academic and legal term[11][12]; are not precisely identical. "Learning difference" represents a commonly accepted term, contributing in the destigmatization of children and adolescents, helping them reveal and communicate to others the difficulties that they face in learning and school performance,

without labeling them as “disordered” [12][68]; or “disabled”, in a sense that the term “learning disability” reveals intellectual disability, formerly mentioned as “mental retardation” [13].

1.2. Type 1 Diabetes Mellitus (T1DM)

Type 1 Diabetes Mellitus (T1DM) in children, is also mentioned as “insulin-dependent” or “juvenile” Diabetes, usually firstly diagnosed during childhood and adolescence, can appear at any age and is a life-long disease. It accounts for about 5% of all patients with diabetes, while its incidence and its prevalence are increasing in the world [69][70][71][72].

Childhood and adolescence are periods characterized by prompt developmental transitions and major changes occurring in the brain, which maybe more vulnerable to extremes of glycemia [73][74]. T1DM with an early onset in young age may have a negative impact on the development of the central nervous system (CNS), reflected in the decrement of cognitive and psychomotor efficiency, mental flexibility and attention; due to secondary conditions (such as chronic hyperglycemia, microvascular abnormalities etc.) [73]. As various prospective studies emphasize, the decline in cognitive functioning is associated more with early onset in young age and microvascular complications (such as retinopathy, nephropathy, neuropathy), than with severe hypoglycemia; while higher HbA1c levels are indicative for mental and psychomotor malfunctioning [73][75]. In addition studies in preschoolers, with severe hypoglycemic episodes at a younger age of 5–7 years old, recorded declines in spatial cognition and information recall, indicative of the susceptibility of the developing CNS to severe hypoglycemia [73][76][77]. Other studies, support that both hypoglycemia and microvascular abnormalities, are risk factors for cognitive malfunctioning [73][76][78][79][80]. Adults with T1DM compared to non-diabetics, presented significant decrease in psychomotor functioning, without any difference occurring in the skills of learning, recall, problem solving [73][79][80][81]. Although numerous studies reveal the association between T1DM and structural-functional changes in CNS, there is no etiological association with specific decline of cognitive efficiency. Research using neuroimaging techniques, such as structural MRI studies, highlighted the lower findings in gray and white substance in population with T1DM compared to non-diabetic peers; associated with severe hyperglycemia, early onset and longer duration of diabetes [73][82]. The clinical manifestations of the reduced white substance in patients with T1DM, were associated with inattention and lower performance in speed of information processing and executive function [73][83]. Age of onset and duration of diabetes, along with microvascular complications in intraparenchymal cerebral arterioles are associated with structural changes, specifically, with white matter lesions (WML) [73][83][84][85][86].

Diagnosis in children can be overwhelming, as symptoms are individualized, occurring differently in each child, especially in the beginning [87][88]; usually including excessive thirst, dehydration, frequent urination, high levels of glucose in the blood and urine, unusual hunger or loss of appetite, fruity breath, tachypnea, nausea, vomiting, abdominal pain, weakness, fatigue, mood changes and irritability, severe diaper rash, yeast infection in girls etc. [87][88]. The American Diabetes Association (ADA) in the Position Statement “Care of Children and Adolescents With Type 1 Diabetes”, published in 2005 [70][89], highlighted the essential differentiations of diabetes with early onset in childhood, from adult diabetes; regarding developmental stage, epidemiology, pathophysiology, as well as care response [70][90][91]. In children and adolescents, the management of diabetes must not be concluded from adult diabetes therapy, but from the awareness of child’s developmental stage and needs, as well as environmental context. Punctual interdisciplinary intervention is a nodal point in preventive care for children and their families [70].

Despite the wealth of data from the significant number of studies reviewed, it is worth noting that children with SLD and T1DM are less frequently researched. Through the narrative review significant issues arose from the data of the recruited research. The themes that were deduced are introduced under distinct titles, highlighting the following three points:

2. The Potential Impact of Diagnosis and Management of T1DM in Children’s Mental Health and Adherence to Insulin Therapy

We are conscious that living with T1DM can be really demanding compared to other chronic conditions. A higher risk of mental comorbidities is linked with T1DM in childhood [93][94][100][101] and adolescence [70][102][103]. Regarding the prevalence of psychological distress, behavioral and mood disorders in population with T1DM, several studies confirm that despite the fact that in childhood, may not differ from the general population, in adolescence the frequency is 2–3 times higher in comparison to non-diabetic peers [70][102][103]. Mental comorbidities may increase disease’s load for both children and carers, worsening metabolic control [94][100][104][105], leading in further deterioration of microvascular

complications and increasing mortality rates [106][107]. Even though most of the children and adolescent patients cope sufficiently with daily glucose controls and insulin treatment, overcome difficulties and withstand challenges, demonstrating incredible resilience [98], some appear to suffer more, experiencing severe mental issues; usually depression, eating disorders [98][108]. Although depression is associated to a moderate degree with maladaptation to treatment of T1DM in children [93], adolescents with depression fail to maintain a sufficient metabolic control, facing a greater risk of exposure to short and long-term complications [98][108][109]. Some studies revealed as predictive factor for psychiatric comorbidities, high HbA1c levels in the early phase of the T1DM onset [94][100]; and highlighted an important clinical problem, estimating that there is a high risk of developing a mental disorder 15–20 years since the T1DM onset (reaching 30% [8]) [94][100]. Psychological well-being is associated with competent metabolic control and a supportive and psychologically healthy environment, that will react timely when depression's symptoms are identified or suspected in a child or an adolescent diagnosed with T1DM, as a responsible adult needs to secure safe diabetes's management and require help from a mental health professional [98].

3. The Potential Impact of T1DM on Cognitive Learning Function and Its Relation to Academic Deficits

Children and adolescent diabetic patients must cope with a demanding and complicated daily routine, concerning blood glucose (BG) levels control, insulin injections, diet and exercise; while continuing to live a "normal life" as their peers do. However, T1DM as a chronic disease along with the stressful BG control and psychosocial effects, is associated with a huge negative impact on school performance [106], inattention and lower spelling performance. The later, was related to greater hyperglycemia exposure [79][80]. For children with SLD and T1DM, daily routine, learning skills and academic attendance are burdened with low cognitive efficiency, due to the coexistence of these two conditions [92].

Numerous studies suggest that although students with T1DM have an average performance on tests of general intelligence, they may demonstrate mild difficulties in cognitive skills, especially in reading [92]. In addition, there is no clear evidence regarding the impact of nearly undetectable neuropsychological deficiency that may occur in children with T1DM, gradually, on their learning skills [92]. Lamentably, there is no substantive data, as the number of studies of learning difficulties in children with T1DM is limited, concerning small and selective samples, using cross-sectional designs, inconsistent control groups and resulting contradictory conclusions [92]. Regarding the performance of this population on specific neuropsychological tests, opposing results are reported, as some studies showed deficits in verbal intelligence [92][110], memory [92][111][112], motor and visuospatial abilities [92][113][114][115]; whereas others identified deficits in abstract/visual reasoning [92][116], attention [92][111][117], work rate and processing speed [92][114]. The T1DM onset before the age of 7 years old [92][111][112][113][118][119] and school absences [92][115][120], are highlighted as risk factors to neuropsychological deficits. The documented subtle neurocognitive impairments among children with T1DMat several ages may not provide assessable detriment in school performance, even gradually [92], in accordance with studies concluding that severe cognitive impairment with a long-term impact in children with T1DM cannot be associated with the effects of diabetes, with the exception of the attribution to hypoglycemic seizures [92][110][111][112][113][114][115][116][117][118][119][120][121].

Despite these findings, monitoring and preventive treatment of hypoglycemia, seizures or coma are essential to secure learning abilities [92].

4. Challenges Related to Diabetes Management for Children and Parents

The successful management of T1DM differs significantly among other chronic diseases in children and adolescents, as it requires along with a high complexity intervention and family involvement; also a supportive school environment [96][97][122]. There's no cure for T1DM and although advances in BG monitoring and insulin delivery have improved patients' quality of life, constant management and ongoing targets and tests can be overwhelming and stressful for both parents and child, as they must learn how to give injections, count carbohydrates and monitor BG.

Diabetes 1 diagnosis constitutes a major crisis for both children and their parents[98]. They experience grief, as they have to confront the life-long nature of the disease and the undercurrent fear of the potential complications [98][123][124][125]. Initially, in the early period, when it is first diagnosed, the young patients usually express sadness, anxiety, irritability, despondency, and negativism in taking insulin or attending school [96][97][98][117][126]. Patients' parents

usually mention that they share with their children feelings of despair, anxiety, along with guilt and worries about the uncertain future [96][97][98][117][126]. These are regular responses that usually occur the first year after diagnosis [96][97][98][117][126]. However, children with underlying maladjustment, may develop in the future, adherence difficulties, psychosocial problems or/ and difficulties in metabolic control [96][126][127], that tend to pick in adolescence [70][94][96][97][98][128]. This could be attributed to the developmental changes that take place during “normal” puberty, such as physiological changes and insulin resistance [70][92][70].

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Keywords

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