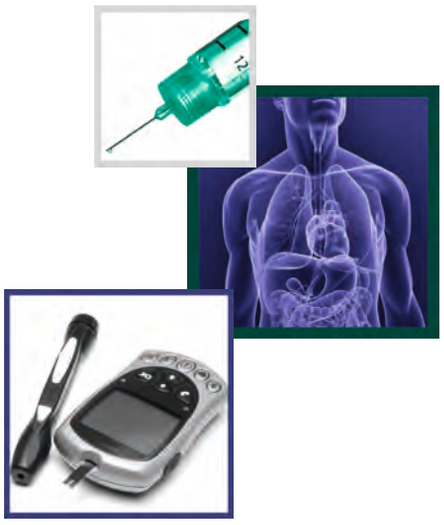
EDITORIAL



Why are young people with diabetes distressed?

Fergus Cameron*

"...the prognosis for our current cohort of young people with Type 1 diabetes has improved significantly. Why then are they so depressed and anxious?"

Recent data from two large international studies (the Finnish Diabetic Nephropathy Study and the Pittsburgh Epidemiology of Diabetes Complications Study) have indicated that the lifespan of current young patients with Type 1 diabetes without kidney disease is close to normal. Other data from numerous sources including the Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications (DCCT/EDIC) studies indicate that diabetic kidney disease is becoming less frequent and will only affect a minority of patients with Type 1 diabetes who are now young. Thus, the prognosis for our current cohort of young people with Type 1 diabetes has improved significantly. Why then are they so depressed and anxious? Data from several Australian research studies and surveys consistently indicate that approximately one in three adolescents and young adults with Type 1 diabetes suffer from significant depression, anxiety or disordered eating behavior [1,2]. This is approximately double the background rate of mental-health disorders in age-matched control groups. Mental-health needs, 'diabetes distress' or 'diabetes burn-out' are also reflected in the 'Statement of Issues' by the Australian consumer group, The Type 1 Diabetes Network [101]. Disturbed mental health is arguably now the leading complication of Type 1 diabetes in this younger group. One of the main questions that has been driving our research activities is why?

There are plenty of existential reasons as to why young people might feel challenged by life with diabetes. There is the omnipresent, Damoclean threat of hypoglycemia, ongoing painful treatment regimens, perceived dietary restrictions, difficulties in balancing a multidimensional condition that can become unstable without warning with a sprinkling of parental guilt as to the origins of an illness that can't be adequately explained. These are all strong and unremitting reasons as to why our patients and their parents (mothers in particular) should feel psychologically challenged by Type 1 diabetes. Thankfully the majority appear to be able to cope with this psychic burden, but for some the challenges are too great. These people must be supported for many reasons not the least of which is that ongoing mental-health issues are a strong predictor of sudden death in diabetic patients in their 20s and 30s [3]. We and others have strongly advocated that mental-health screening should be part of routine care for young people with diabetes, particularly before their transition to adult services [4].

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There is also an increasing body of evidence that Type 1 diabetes in childhood affects the brain directly. Glucose is the primary cellular fuel of the brain and sudden changes in blood glucose can be associated with mood swings. Irritability, short-temperedness and aggression are associated with hyperglycemia in particular [5–7]. Several investigators have shown that both high and low levels of blood glucose acutely reduce the ability to perform academically (problem solving, etc.) in Type 1 diabetes patients [8–10]. Initially there was some assurance that chronic impacts of Type 1 diabetes on cognition were minimal. An 18 year follow-up study of the adolescent cohort of the DCCT failed to show any significant cognitive deterioration [11]. The salient point however, is that this study was designed to measure the within-patient impact of intensive therapy upon cognitive outcomes in the medium term. It was not designed to measure the impact of Type 1 diabetes over the period of neuromaturation compared with nondiabetic children, particularly in those diagnosed under the age of 5 years. The youngest member of the DCCT adolescent cohort was 13 years of age at the time of study entry, with most being in mid- to late-adolescence, well after the period of maximal neural sensitivity to ontogenic disturbance. A number of subsequent studies observing younger patients and comparing them with normative data have shown that continued exposure to hyper- and hypoglycemia over time unfortunately does appear to have cumulative impacts on brain development. In particular significant hypoglycemia (associated with loss of consciousness) under the age of 5 years and episodes followed by prolonged periods of hyperglycemia and diabetic ketoacidosis appear to adversely impact upon normal brain development [12–16].

From a functional point of view, several studies grouped school performances of Type 1 diabetes patients at preschool, primary school and secondary school levels show that they perform less well than nondiabetic children [14,17,18]. Disturbing nationwide data from Sweden shows that children with Type 1 diabetes perform significantly more poorly at year 12 equivalent exams than their nondiabetic peers [18]. In a 12 year follow-up study undertaken by our group we studied children from the time of diabetes diagnosis to the point of brain maturation in their early 20s. We compared our diabetic patients with a control group of children who were identical in terms of IQ, socioeconomic status and gender balance at the time of diagnosis. Twelve years later at the time of neuromaturation our diabetic patients had significantly decreased scores on full-scale IQ, verbal IQ and working memory compared with the control group [13]. The diabetic group also had twice the rates of mental health disorder and failure of secondary school completion compared with the control group [1,19]. Brain MRI studies of this diabetic cohort showed significant alterations in some regions of brain biochemistry consistent with lower levels of neuronal density and brain injury, particularly in the frontal regions [13]. Interestingly cross-sectional MR studies from the Joslin in adults with Type 1 diabetes ranging from 25–40 years of age compared with age-matched controls showed no differences in white matter but lower grey matter volumes in several brain regions also involving the frontal gyri [20].

Another example of integrated brain function in childhood is behavior. Longitudinal studies have shown that behavioral problems seen in children with Type 1 diabetes tend to persist. In our research, behavioral problems seen shortly after diagnosis were strongly predictive 12 years later of mental health problems, poorer lifetime metabolic control, lower study/work participation and failure of transition with crisis-only diabetes care. Others have shown that behavioral problems in late adolescence and young adulthood are predictive of metabolic control and behavioral problems in mid-adulthood [21]. Thus, the significance of disturbed mental health and behavior at the time of neuromaturation is not simply a moment of transient adolescent angst. There appears to be a trajectory continuum whereby behavioral problems in early-to-mid childhood are predicative of behavioral, mental health and clinical outcomes in late adolescence which are predictive of clinical and mental health outcomes in mid-adulthood.

Given that all people with diabetes continuously experience high, low and fluctuating levels of blood glucose it is difficult to isolate the aspects of blood-glucose control that are the most important in brain development. These analyses are further complicated by insulin and counter-regulatory hormones also having direct and glucose-independent effects upon the brain [22,23]. From a systems and functional point of

view though, structural equation modeling studies indicate that frontal lobe executive functioning determines adherence in diabetes care, which in turn predicates glycemic control [24]. Thus, regardless of the mechanisms and hierarchy of cellular insults in developing brains, the unstable metabolic milieu of Type 1 diabetes appears to impede executive brain function, which in turn begets further metabolic instability and potential ongoing neuronal injury – a self-perpetuating cycle of glycemic instability creating further glycemic instability via a neurobehavioral pathway.

In the past 15–20 years since the DCCT, standards of care have improved vastly for young people with Type 1 diabetes. The corollary of this is that we now rarely see evidence of traditional diabetes complications such as kidney and eye disease in pediatric diabetes clinics. This has allowed us to focus upon a broader suite of neurocognitive and psychosocial diabetes outcomes. The challenge is now to research strategies that protect developing brains in children with diabetes and to support those with behavioral and mental-health problems. Thus, the new frontier in pediatric diabetes healthcare is now to optimize those pre-eminent developmental tasks of childhood and adolescence brain development and psychological wellbeing.

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■ Website

101 'Statement of Issues' by the Type 1 Diabetes Network. www.d1.org.au/issues-statement/issues-statement.html (Accessed 2 November 2011)