# Screening for psychological disorders in youth with Type 1 diabetes: who, when, what and how?

FJ Cameron*[1] & EA Northam[2,3]

**Practice Points**

- Screening for psychological disorders in youth with Type 1 diabetes should be an integral part of 'gold-standard' clinical practice.
- Who to screen: preferably an all-of-clinic approach should be used given the high prevalence; however, priority should be given to younger children exhibiting externalizing behavior disorders or adolescents exhibiting chronic poor metabolic control or emotional disorders.
- When is screening likely to be most efficacious: screening should be carried out at any time, but if resources are constrained, either shortly after diagnosis or in midadolescence, it should be 2–3 years prior to transition to adult services.
- What disorders to screen for: in younger children, parent–child conflict should be investigated; in adolescents, affective disorders (depression and anxiety) and eating disorders are the most likely psychological problems.
- How best to screen: there are a number of validated self-report questionnaires including the Child Behavior Checklist for younger children and the Youth Self Report for adolescents.

**SUMMARY** Psychological morbidity is significantly more common in youth with Type 1 diabetes than microvascular and autoimmune complications. As such, mental health problems represent a considerable burden to both the individual and the public health system. Risk factors for psychological distress in youth with this disease are identified and the long-term adverse consequences of poorly controlled diabetes are highlighted. A practical and cost-effective case is made for clinic-based screening at key time points to identify troubled youth and to facilitate timely intervention for this 'at risk' population.

Adverse mental health outcomes are arguably now the leading 'complication' of Type 1 diabetes (T1D) during childhood and adolescence. Whereas contemporary microvascular and autoimmune comorbidities occur at rates of only 0–6% [1,2], there are numerous reports of either mental health disorder or self-reported mental health referral in as many as 20–50% of youth and young adults with diabetes [3–9], although not all studies report significant elevations in

[1]Departments of Endocrinology & Diabetes, Royal Children's Hospital, Parkville, Melbourne, VIC 3052, Australia
[2]Department of Psychology, Royal Children's Hospital, Murdoch Childrens Research Institute, Parkville, Melbourne, VIC 3052, Australia
[3]Departments of Pediatrics & Psychology, The University of Melbourne, Melbourne, Australia
*Author for correspondence: Tel.: +61 3 9345 5951; Fax: +61 3 9347 7763; fergus.cameron@rch.org.au

Future Medicine part of fsg

psychopathology (e.g., [10]). A recent meta-analysis [11] confirmed an overall elevated risk for parent-reported psychological distress (medium effect size of 0.6) in children with T1D with a lower, but still significant, increase of self-reported depression (medium effect size of 0.4). We have previously advocated that such a high prevalence rate merits routine screening [12]. Given that a minority of pediatric diabetes centers have dedicated psychology support [13,14], a shift to a mental health focus in diabetes complications screening has substantial implications for care and service delivery. It would be highly desirable if routine mental health screening was integrated into usual diabetes care, but in the context of the almost universal experience of limited resources, the question remains as to how this is best achieved. In this paper, we provide a template to help clinicians recognize early symptoms of psychological distress and to be alert to times of increased vulnerability for their young patients. We suggest practical and cost-effective approaches to clinic-based screening for mental health problems to facilitate the goal of timely intervention before problems become entrenched and secondary sequelae of the initial problem (e.g., school absence, family conflict, social withdrawal and poor metabolic control) result in greatly increased morbidity. Such an approach assumes that mental health expertise and resources are an integral part of the treating team, but are at least available on a referral basis. In essence, the critical issues for such intervention are: who to screen?; when is screening likely to be most efficacious?; what disorders to screen for?; and how best to screen?

## Who should be screened for psychological dysfunction?

There has been much research into identifying the antecedents and markers of psychological distress in youth with T1D. This has allowed us to predict who is likely to be at risk of developing or currently having a psychological disorder. Adjustment problems that commonly occur at or around the time of diabetes diagnosis [15], have been found by several groups to predict later psychological difficulties [4,16,17]. Prospective, longitudinal research by our group from the time of diagnosis to the age of neuromaturation is supportive of these research findings. Externalizing behaviors (oppositional defiant behavior and conduct problems) already evident at diagnosis, were associated with a significantly greater likelihood of a Diagnostic and Statistical Manual of Mental Disorders (4th Edition) diagnosis during adolescence [7], and greater need for mental health services at some point over the course of the illness when followed up 12 years post-diagnosis [9]. These findings are not unique to the context of childhood diabetes and are consistent with the developmental psychopathology literature in general [18–20], which suggests that untreated, early-onset behavior problems tend to persist and generalize into broader and more serious forms of psychopathology.

Of course, not all patients will be diagnosed in childhood; therefore, adolescent markers are equally desirable. Poor adherence to diabetes-related tasks is commonly associated with poor mental health – particularly depression and eating disorders [21–23]. For example, in one study of youth aged 8–21 years, 56% of those with psychiatric disorders, compared with only 17% without a disorder, failed to comply with their medical regimen [24]. Compromised adherence in youth with psychological problems is, in turn, associated with poor metabolic control. Treating HbA1c values as a continuum, one study of youth with diabetes showed that for each rise in HbA1c of 1%, there was a 27% increased probability of depression [23]. Alternatively, using a threshold HbA1c, another study showed that youth with HbA1c levels above 9.0% were twice as likely to exhibit higher levels of aggression, delinquent behaviors and attention problems [25]. Depression and behavior problems have also been associated with increased risk of multiple diabetes-related hospitalizations [16,26,27]. However, associations between psychological maladjustment and poor metabolic control in youth with diabetes are not straightforward. While some individuals experience stress-related neurohormonal changes that may adversely influence metabolic control directly through endocrine pathways [28–30], in other individuals, high anxiety and other internalizing symptoms are associated with better adherence and better glycemic control [31–34]. Of course, association implies neither cause nor effect, and these findings are consistent with neurotic symptoms either contributing to, or resulting from, obsessive preoccupation with the demands of the diabetes treatment regimen or, indeed, both. In a study of 235 children with diabetes, structural equation modeling indicated that metabolic control was underpinned by adherence to diabetes-related tasks, which in turn was associated with executive functioning (planning, organization and problem solving skills) and behavior [35]. This

linear model, however, does not allow for the possibility of poor metabolic control impacting upon executive skills and behavior.

A constant supply of glucose to the brain is critical for normal cerebral metabolism, with both hypoglycemia and hyperglycemia affecting activity, survival and function of neural cells in *in vitro* and *in vivo* models [36–39]. Furthermore, we have recently shown that fluctuating glycemia in an *in vitro* model redolent of unstable diabetes, may be more neurotoxic than either sustained hyper- or hypo-glycemia [40]. In children, acute hyperglycemia is associated with higher levels of externalizing behavior problems, low mood [41,42] and impaired cognition [43,44]. Long-term glycemic instability, during childhood (and neurodevelopment) is associated with impaired cognition, with both severe hypoglycemic events [45–48] and chronic hyperglycemia [46,49–51] implicated in this association. Even at the time of diagnosis (with or without diabetic ketoacidosis), impaired mental state is associated with a significantly lower full scale IQ in the medium term [52]. Subtle cognitive deficits, often poorly recognized and remediated, are likely to contribute to poorer school performance evident in children with diabetes [9,53], which in turn increases risks for low self-esteem, anxiety and behavioral difficulties. Thus, glycemic instability and poor metabolic control in childhood appear to be injurious to the brain with impacts upon cognition, affect and behavior. Whilst mediating factors such as coping style, locus of control, social supports and parental psychopathology may contribute to the inconsistent relationship between mental health and metabolic control, the weight of the literature supports the notion of a neurobehavioral feedback 'double jeopardy' relationship between psychological and physiologic well being.

When resources allow, it would be preferable to screen all children and youth with diabetes for mental health disorders; however, when resources are constrained, a more focused approach can be adopted. Young children exhibiting adjustment and oppositional behaviors, or older youth exhibiting obvious psychopathological signs, poor coping strategies or problems with adherence and/or metabolic control should be considered at greater risk of an overt or latent psychological disorder. One might also include children with very 'tight' control as targets for screening, as over-diligent preoccupation with the treatment regimen may be masking covert anxiety or depression. Finally, clinicians should be aware of contextual events, such as family breakdown, or physical or mental ill health in parents or other family members, as previously well-adjusted children may decompensate in the face of these additional stresses.

## When should screening be undertaken?

This question can be addressed by either assessing the likelihood of yield (detecting incident cases) or the gravity of clinical consequence. Fortunately in the context of T1D in youth, these two imperatives often coincide. Good clinical care demands that symptoms of psychological distress should be responded to on an 'as needed' basis whenever they are present. However, current evidence suggests two key periods when routine screening of the diabetes clinic population may significantly reduce individual and family distress, and provide a window of opportunity to offer evidence-based interventions. In turn, this approach should reduce longer-term psychological and physical health morbidity, with obvious benefit both to the individual, as well as to the public health budget.

The time around diagnosis of T1D in a child is likely to be associated with high levels of contact with the treating team. Both the child and family experience a period of considerable adjustment to the new challenge of managing a demanding chronic illness, which draws heavily on the family's capacity to establish organized routines, to communicate and problem solve effectively and to provide high levels of emotional support. A pre-existing history of oppositional behavior problems in the younger child is an obvious risk factor for poor adjustment and heightened levels of parent–child conflict around diabetes management tasks. It is clear from our own findings [7,9], and from the developmental psychopathology literature in general, that externalizing behaviors in the young child tend to persist and generalize into internalizing symptoms by adolescence. In addition, parental motivation to address problems and make changes is likely to be high around the time of diagnosis, thus routine screening and targeted intervention at this time is likely to be met by a positive response from families.

Adolescence is a period where there is an increased mental health burden in youth with chronic illness [54]. Youth with diabetes contribute to this increase in prevalence, having referral rates for mental health services that are approximately twice the rate of healthy controls [9]. The clinical imperative of detecting mental health disorders in adolescents with diabetes cannot be overstated. Apart from the immediate-term double jeopardy

association of poor metabolic control with poor mental health, there are equally significant longer-term associations. First, mental health difficulties in late adolescence are associated with lower rates of work/study participation and higher rates of unsuccessful transition to adult diabetes care [9]. Second, the decade of greatest risk of sudden, unexplained diabetes-related death is between 20 and 30 years of age [55]. A past history of mental health disorder in adolescence increases the odds ratio of sudden death 4.6-fold [55]. Finally, untreated mental health issues do not resolve spontaneously. Mental health issues in adolescence persist into midadulthood and are associated with poorer metabolic control throughout life [6,56]. Allowing for the above points, it appears reasonable to select adolescence as a key time to screen for latent or overt mental health issues. Obviously, serial screening during this time would be optimal; however, if one were to screen for mental health issues on only one occasion during this period, a strong case can be made for a time point in midadolescence, 2–3 years prior to transition. This fulfils the imperatives of yield and clinical significance, whilst allowing sufficient time for intervention to occur prior to leaving pediatric care.

## What psychological disorders should be screened for?

Given the high demand for effective family communication in diabetes management, parent–child conflict and oppositional behavior in the younger child with diabetes are obvious foci of screening programs early in the natural history of the disease. This is critical, as there is empirical evidence in the developmental psychopathology literature that behavior problems in the child can be effectively treated if intervention occurs early [18–20]. Enhancing parenting skills and reducing family conflict appears to increase the effectiveness of early intervention to address behavior problems in the younger child [57] and may reduce the risk of a secondary or comorbid internalizing disorder in adolescence. Furthermore, externalizing behaviors are easily and reliably identified by parents using simple and cost-effective standardized questionnaires that lend themselves to administration within a diabetes outpatient clinic.

Developmental transitions, such as the onset of puberty, offer new challenges, as well as opportunity for positive change. In addition, in youth with diabetes, adolescence marks an important transition to increased autonomy in disease management. Optimal control requires a focus on long-term goals, as well as intact executive functions, which are not fully mature in many adolescents [35]. This mismatch between the adolescent's desire for autonomy and a still evolving capacity for foresight and sound judgment is likely to increase parental anxiety and may exacerbate parent–child conflict. Multiple informants and comprehensive screening measures are required for this age group, as symptom expression covers a broad spectrum, with increased risks for affective and eating disorders, sometimes not known to parents, as well as conduct problems [7,54]. In addition to reducing mental health symptoms in this age group, there is a need to proactively enhance self-esteem and coping skills. That is, effective intervention with youth requires a focus on both symptom reduction, as well as screening and proactive enhancement of adaptive coping skills to support good mental health and to equip the adolescent to meet the new challenges of greater independence and autonomy in daily life and disease management. Thus, there is a clear need for a multidimensional view of psychological well being in this age group and a flexible response to problems when they present, either opportunistically in routine clinical care or through more formal screening. Our own clinic [Serlachius A. The best of coping: a randomised trial to improve glycaemic control and psychosocial well-being in adolescents with Type 1 diabetes (2012), Unpublished Data], and others [58], have demonstrated the efficacy of clinic-wide preventative or skill-enhancing interventions. Other children with more serious psychopathology and those presenting against a background of family dysfunction, will require a multidisciplinary team approach and an individualized treatment plan.

As noted above, clinicians should also be aware of the possibility of cognitive impairment that may be associated with adverse behavioral and emotional outcomes. In adults with T1D, elevated prefrontal cortical glutamate-glutamine-γ-aminobutyric acid levels detected on magnetic resonance spectroscopy were associated with poorer cognitive outcomes and mild depression [59]. Subtle impairments in verbal and full-scale IQ, as well as deficits in executive skills, memory and attention have been reported in pediatric cohorts, particularly in children diagnosed with diabetes early in life [46,48,49]. There is an increasing body of evidence highlighting morphologic and spectroscopic brain changes with [60,61] and

without [62–65] cognitive assessment in children and adolescents with diabetes, although direct associations between these changes and emotional status are yet to be reported. Morphologic findings have varied within the diabetic cohorts studied; however, most groups found associations between a history of severe hypoglycemia and regional gray matter volumes [60–62,65]. Given the relatively high rates of coexisting cognitive and emotional pathology in diabetic youth, it is not unreasonable to assume that there may be associations. Thus, it may prove to be the case that some patients who have been repeatedly exposed to extremes of glycemia and acidosis with apparent psychopathology, may be best approached using a neurodisability, rather than a primarily behavioral/emotional paradigm.

## How is screening best performed?

One of the great benefits of tertiary diabetes care in most pediatric centers is continuity of care. This allows for repeated review of patients and for age- and developmental stage-appropriate care to be delivered. The process of ongoing review also allows for screening tools to be used that may have a lower sensitivity than would otherwise be necessary, as questionnaire responses can be combined with clinician knowledge, based on an ongoing relationship with the child and family. Parent report of childhood behavior problems using standardized pencil and paper questionnaires, such as the Child Behavior Checklist [66], the Behavior Assessment System for Children [67] or the Strengths and Difficulties Questionnaire [68], have proven reliable and valid, as well as being cost effective and easy to administer within a diabetes clinic. Broad-spectrum measures such as these can be followed by more targeted clinical assessment and clinical intervention for any problems identified, thus facilitating the most effective use of scarce and expensive clinical resources.

Adolescence marks an important developmental transition when self-report of symptoms is critical to reliably ascertain mental health difficulties, particularly internalizing symptoms that may go unnoticed by parents. The Behavior Assessment System for Children and the Strengths and Difficulties Questionnaire have self-report forms normed for the adolescent age group and there are upward extensions of the Child Behavior Checklist, namely the Youth Self-Report and the Young Adult Self Report that can be used alone or in conjunction with a parent report. The Beck Youth Inventory assesses symptoms of depression, anxiety, anger, disruptive behavior and self-concept in a measure targeted specifically for the adolescent age group [69]. Consideration might also be given to screening diabetes-related quality of life in this age group to identify negative feelings and barriers to treatment adherence.

## Conclusion

Any clinician involved in the care of children and adolescents with T1D can attest to the difficulties in managing intercurrent emotional, psychiatric and behavioral problems. Some of these difficulties will arise from a lack of resourcing of psychological support, a lack of consensus as to defined psychological assessment pathways or to a lack of training for physicians in the recognition of mental health difficulties. The possibility of associated cognitive impairment, specifically in the areas of memory and attention, which are critical areas for successful participation in a learning environment, further adds to diagnostic and management complexity. However, notwithstanding variability in cultural and clinical contexts, it is possible to define potential starting points – the 'who', 'when', 'what' and 'how' of a psychological screening program.

## Future perspective

As a starting point, we argue for basic training in the recognition of psychological difficulties for all clinicians involved in front-line care of children with T1D, a targeted and systematic approach to clinic-based screening and access to mental health expertise to interpret screening measures. Specific models of mental health service delivery to support clinical care of children with T1D, the treatment modalities most efficacious for particular problems and the barriers to treatment remain significant challenges to be addressed, as a matter of some urgency, if we are to significantly reduce the well-documented psychological morbidity associated with this disease and its implications for optimal metabolic control in the future.

## Financial & competing interests disclosure

*The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.*

*No writing assistance was utilized in the production of this manuscript.*

## References


Papers of special note have been highlighted as:

- ■ of interest
- ■■ of considerable interest

1 Mohsin F, Craig ME, Cusumano J *et al.* Discordant trends in microvascular complications in adolescents with Type 1 diabetes from 1990 to 2002. *Diabetes Care* 28(8), 1974–1980 (2005).

2 Kong A, Donath S, Harper CA, Werther GA, Cameron FJ. Rates of diabetes mellitus-related complications in a contemporary adolescent cohort. *J. Pediatr. Endocrinol. Metab.* 18(3), 247–255 (2005).

3 Lavigne JV, Faier-Routman J. Psychological adjustment to pediatric physical disorders: a meta-analytic review. *J. Pediatr. Psychol.* 17(2), 133–157 (1992).

4 Kovacs M, Goldston D, Obrosky DS, Bonar LK. Psychiatric disorders in youths with IDDM: rates and risk factors. *Diabetes Care* 20(1), 36–44 (1997).

■ **Excellent overview of risk factors and prevalence rates of mental health problems in youth with diabetes.**

5 Kovacs M, Obrosky DS, Goldston D, Drash A. Major depressive disorder in youths with IDDM. A controlled prospective study of course and outcome. *Diabetes Care* 20(1), 45–51 (1997).

6 Bryden KS, Peveler RC, Stein A, Neil A, Mayou RA, Dunger DB. Clinical and psychological course of diabetes from adolescence to young adulthood: a longitudinal cohort study. *Diabetes Care* 24(9), 1536–1540 (2001).

■■ **Tracks the continuity of mental health problems from adolescence to young adulthood and the associated risks for poor metabolic control.**

7 Northam EA, Matthews LK, Anderson PJ, Cameron FJ, Werther GA. Psychiatric morbidity and health outcome in Type 1 diabetes – perspectives from a prospective longitudinal study. *Diabet. Med.* 22(2), 152–157 (2005).

■■ **Describes psychiatric morbidity in an adolescent sample followed longitudinally from diagnosis 10 years previously and its relationship to metabolic control history.**

8 Hislop AL, Fegan PG, Schlaeppi MJ, Duck M, Yeap BB. Prevalence and associations of psychological distress in young adults with Type 1 diabetes. *Diabet. Med.* 25(1), 91–96 (2008).

9 Northam EA, Lin A, Finch SJ, Werther GA, Cameron FJ. Psychosocial well-being and functional outcomes in youth with Type 1 diabetes 12 years after disease onset. *Diabetes Care* 33(7), 1430–1437 (2010).

■■ **Mental health, metabolic control history and functional outcomes (school completion, current work/study participation and transition to adult diabetes care) in youth with Type 1 diabetes, compared with community controls in a prospective study from diabetes onset.**

10 Helgeson VS, Snyder PR, Escober O, Siminerio L, Becker D. Comparison of adolescents with and without diabetes on indices of psychosocial functioning for 3 years. *J. Pediatr. Psychol.* 32, 794–806 (2007).

11 Reynolds KA, Hekgeson VS. Children with diabetes compared with peers: depressed? Distressed? *Ann. Behav. Med.* 42, 29–41 (2011).

■■ **Recent meta-analysis of psychological morbidity based on both parent and child reports, highlighting the moderately increased risk of psychological distress in general and the mild-to-moderate elevations in affective disorders (anxiety and depression).**

12 Cameron FJ, Northam EA, Ambler G, Daneman D. Routine psychological screening in youth with Type 1 diabetes and their parents: a notion whose time has come? *Diabetes Care* 30(10), 2716–2724 (2007).

■■ **Reviews the arguments for systematic, clinic-based screening of mental health problems in youth with diabetes and discusses evidence of efficacy for various approaches.**

13 Jefferson IG, Swift PG, Skinner TC, Hood GK. Diabetes services in the UK: third national survey confirms continuing deficiencies. *Arch. Dis. Child.* 88(1), 53–56 (2003).

14 Skinner TC, Cameron FJ. Improving metabolic control in children: what aspects of therapy really matter? *Diabet. Med.* 27(4), 369–375 (2010).

■■ **Argues that the recent focus on pharmaco-technological advances in treatment regimens has occurred at the expense of a focus on psychosocial support, goal setting and team cohesion.**

15 Kovacs M, Feinberg TL, Paulauskas S *et al.* Initial coping responses and psychosocial characteristics of children with insulin-dependent diabetes mellitus. *J. Pediatr.* 106(5), 827–834 (1985).

16 Charron-Prochownik D, Kovacs M, Obrosky DS, Stiffler L. Biomedical and psychosocial predictors of early rehospitalisation among children with insulin-dependent diabetes mellitus: a longitudinal study. *Diabet. Med.* 11(4), 372–377 (1994).

17 Maharaj S, Daneman D, Olmsted M, Rodin G. Metabolic control in adolescent girls: links to relationality and the female sense of self. *Diabetes Care* 27(3), 709–715 (2004).

18 Rutter M, Sroufe LA. Developmental psychopathology: concepts and challenges. *Dev. Psychopathol.* 12(3), 265–296 (2000).

19 Cicchetti D, Rogosch FA. A developmental psychopathology perspective on adolescence. *J. Consult. Clin. Psychol.* 70(1), 6–20 (2002).

20 Hinshaw SP. Process, mechanism and explanation related to externalising behaviour in developmental psychopathology. *J. Abnorm. Child. Psychol.* 30(5), 431–446 (2002).

21 Goldston DB, Kelley AE, Reboussin DM *et al.* Suicidal ideation and behaviour and noncompliance with the medical regimen among diabetic adolescents. *J. Am. Acad. Child. Adol. Psychiatry* 36(11), 1528–1536 (1997).

22 Maronian S, Vila G, Robert J, Mouren-Simeoni M. Troubles DSM-IV, quilibre metabolique et complications somatiques dans le diabete insulino-dependant de l"enfant et de l' adolescent. *Ann. Medico Psychologiques* 157, 320–331 (1999).

23 Hassan K, Loar R, Anderson BJ, Heptulla RA. The role of socioeconomic status, depression, quality of life, and glycemic control in Type 1 diabetes mellitus. *J. Pediatr.* 149(4), 526–531 (2006).

24 Kovacs M, Goldston D, Obrosky S, Iyengar S. Prevalence and predictors of pervasive non-compliance with medical treatment among youths with insulin-dependent diabetes mellitus. *J. Am. Acad. Child. Adol. Psychiatry* 31(6), 1112–1119 (1992).

25 Leonard BJ, Jang YP, Savik K, Plumbo PM, Christenson R. Psychosocial factors associated with levels of metabolic control in youth with Type 1 diabetes. *J. Pediatr. Nurs.* 17(1), 28–37 (2002).

26 Seiffge-Krenke I, Stemmler M. Coping with everyday stress and links to medical and psychosocial adaptation in diabetic adolescents. *J. Adolesc. Health* 33(3), 180–188 (2003).

27 Stewart SM, Rao J, Emslie GJ, Klein D, White PC. Depressive symptoms predict hospitalization for adolescents with Type 1 diabetes mellitus. *Pediatrics* 115(5), 1315–1319 (2005).

28 Schade DS, Eaton RP. The temporal relationship between endogenously secreted stress hormones and metabolic decompensation in diabetic man. *J. Clin. Endocrinol. Metab.* 50(1), 131–136 (1980).

29 Shamoon H, Hendler R, Sherwin RS. Altered responsiveness to cortisol, epinephrine and glucagon in insulin-infused juvenile-onset diabetes. *Diabetes* 29(4), 284–291 (1980).

30 Chase HP, Jackson GG. Stress and sugar control in children with insulin-dependent diabetes mellitus. *J. Pediatr.* 98(6), 1011–1013 (1981).

31 Grey M, Cameron M, Lipman TH, Thurber FW. Psychosocial status of children with diabetes in the first 2 years after diagnosis. *Diabetes Care* 18(10), 1330–1336 (1995).

32 Cohen DM, Lumley MA, Naar-King S, Partridge T, Cakan N. Child behavior problems and family functioning as predictors of adherence and glycemic control in economically disadvantage children with Type 1 diabetes: a prospective study. *J. Pediatr. Psychol.* 29(3), 171–184 (2004).

33 Kovacs M, Ho V, Pollock MH. Criterion and predictive validity of the diagnosis of adjustment disorder: a prospective study of youths with new-onset insulin-dependent diabetes mellitus. *Am. J. Psychiatry* 152(4), 523–528 (1995).

34 Daviss WB, Coon H, Whitehead P, Ryan K, McMahon W. Predicting diabetic control from competence, adherence, adjustment, and psychopathology. *J. Am. Acad. Child. Adolesc. Psychiatry* 34(12), 1629–1636 (1995).

35 McNally K, Rohan J, Pendley JS, Delamater A, Drotar D. Executive functioning, treatment adherence, and glycemic control in children with Type 1 diabetes. *Diabetes Care* 33(6), 1159–1162 (2010).

36 Russo VC, Kobayashi K, Najdovska S, Baker NL, Werther GA. Neuronal protection from glucose deprivation via modulation of glucose transport and inhibition of apoptosis: a role for the insulin-like growth factor system. *Brain Res.* 1009(1–2), 40–53 (2004).

37 Kobayashi K, Xin Y, Ymer SI, Werther GA, Russo VC. Subtractive hybridisation screen identifies genes regulated by glucose deprivation in human neuroblastoma cells. *Brain Res.* 1170, 129–139 (2007).

38 Tomlinson DR, Gardiner NJ. Glucose neurotoxicity. *Nat. Rev. Neurosci.* 9(1), 36–45 (2008).

39 Sima AA. Encephalopathies: the emerging diabetic complications. *Acta Diabetol.* 47(4), 279–293 (2010).

40 Russo V, Higgins S, Werther GA, Cameron FJ. Effects of fluctuating glucose levels on neuronal cells *in vitro*. *Neurochem. Res.* 37(8), 1768–1782 (2012).

41 Martin DD, Davis EA, Jones TW. Acute effects of hyperglycaemia in children with Type 1 diabetes mellitus: the patient's perspective. *J. Pediatr. Endocrinol. Metab.* 19(7), 927–936 (2006).

42 McDonnell CM, Northam EA, Donath SM, Werther GA, Cameron FJ. Hyperglycaemia and externalising behaviour in diabetic children. *Diabetes Care* 30(9), 2211–2215 (2007).

43 Davis EA, Soong SA, Byrne GC, Jones TW. Acute hyperglycaemia impairs cognitive function in children with IDDM. *J. Pediatr. Endocrinol. Metab.* 9(4), 455–461 (1996).

44 Gonder-Frederick LA, Zrebiec JF, Bauchowitz AU *et al.* Cognitive function is disrupted by both hypo- and hyperglycemia in school-aged children with Type 1 diabetes: a field study. *Diabetes Care* 32(6), 1001–1016 (2009).

45 Hershey T, Lillie R, Sadler M, White NH. A prospective study of severe hypoglycaemia. *Pediatr. Diabetes* 5(2), 63–71 (2005).

46 Perantie DC, Lim A, Wu J *et al.* Effects of prior hypoglycaemia and hyperglycaemia on cognition in children with Type 1 diabetes mellitus. *Pediatr. Diabetes* 9(2), 87–95 (2008).

47 Asvold BO, Sand T, Hestad K, Bjørgaas MR. Cognitive function in Type 1 diabetic adults with early exposure to severe hypoglycemia: a 16-year follow-up study. *Diabetes Care* 33(9), 1945–1947 (2010).

48 Lin A, Northam EA, Rankins D, Werther GA, Cameron FJ. Neuropsychological profiles of young people with Type 1 diabetes 12 yr after disease onset. *Pediatr. Diabetes* 11(4), 235–243 (2010).

49 Shehata G, Eltayeb A. Cognitive function and event-related potential in children with Type 1 diabetes. *J. Child. Neurol.* 25(4), 469–474 (2010).

50 Patina-Fernandez AM, Delamater AM, Applegate EB *et al.* Neurocognitive functioning in preschool-age children with Type 1 diabetes mellitus. *Pediatr. Diabetes* 11(6), 424–430 (2010).

51 Kaufmann L, Pixner S, Starke M *et al.* Neurocognition and brain structure in pediatric patients with Type 1 diabetes. *J. Pediatr. Neuroradiol.* 1(1), 25–35 (2012).

52 Nadebaum C, Scratch SE, Northam EA, Cameron FJ. Clinical utility of mental state screening as a predictor of intellectual outcomes six months after diagnosis of Type 1 diabetes. *Pediatr. Diabetes* doi:10.1111/j.1399-5448.2012.00870.x (2012) (Epub ahead of print).

53 Dahlquist G, Källén B, Swedish Childhood Diabetes Study Group. School performance in children with Type 1 diabetes – a population-based register study. *Diabetologia* 50(5), 957–964 (2007).

54 Wallander JL, Varni JW. Effects of pediatric chronic physical disorders on child and family adjustment. *J. Child. Psychol. Psychiatry* 39(1), 29–46 (1998).

55 Laing SP, Jones ME, Swerdlow AJ, Burden AC, Gatling W. Psychosocial and socioeconomic risk factors for premature death in young people with Type 1 diabetes. *Diabetes Care* 28(7), 1618–1623 (2005).

56 Bryden KS, Dunger DB, Mayou RA, Peveler RC, Neil HA. Poor prognosis of young adults with Type 1 diabetes: a longitudinal study. *Diabetes Care* 26(4), 1052–1057 (2003).

57 Sanders MR, Markie-Dadds C, Tully LA, Bor W. The triple p-positive parenting program: a comparison of enhanced, standard, and self-directed behavioural family intervention for parents of children with early onset conduct problems. *J. Consult. Clin. Psychol.* 68(4), 624–640 (2000).

58 Nansel TR, Iannotti RJ, Liu A. Clinic-integrated behavioural intervention for families of youth with Type 1 diabetes: randomised clinical trial. *Pediatrics* 129(4), e866–e873 (2012).

59 Lyoo IK, Yoon SJ, Musen G *et al.* Altered prefrontal glutamate-glutamine-γ-aminobutyric acid levels and relation to low cognitive performance and depressive symptoms in Type 1 diabetes mellitus. *Arch. Gen. Psychiatry* 66(8), 878–887 (2009).

60 Northam EA, Rankins D, Lin A *et al.* Central nervous system function in youth with Type 1 diabetes 12 years after disease onset. *Diabetes Care* 32(3), 445–450 (2009).

61 Aye T, Reiss AL, Kesler S *et al.* The feasibility of detecting neuropsychologic and neuroanatomic effects of Type 1 diabetes in young children. *Diabetes Care* 34(7), 1458–1462 (2011).

62 Perantie DC, Wu J, Koller JM *et al.* Regional brain volume differences associated with hyperglycemia and severe hypoglycemia in youth with Type 1 diabetes. *Diabetes Care* 30(9), 2331–2337 (2007).

63 Hershey T, Perantie DC, Wu J, Weaver PM, Black KJ, White NH. Hippocampal volumes in youth with Type 1 diabetes. *Diabetes* 59(1), 236–241 (2010).

64 Perantie DC, Koller JM, Weaver PM *et al.* Prospectively determined impact of Type 1 diabetes on brain volume during development. *Diabetes* 60(11), 3006–3014 (2011).

65 Pell GS, Lin A, Wellard RM *et al.* Age-related loss of brain volume and T2 relaxation time in youth with Type 1 diabetes. *Diabetes Care* 35(3), 513–519 (2012).

66 Achenbach TM, Rescorla LA. *Manual for the ASEBA School-Age Forms and Profiles.* University of Vermont, Research Center for Children, Youth, and Families. VT, USA (2001).

67 Reynolds CR, Kamphaus RW. *BASC-2 (Behavioral Assessment System for Children, 2nd Edition)*. NCS Pearson, Inc., MN, USA (2004).

68 Goodman R. The Strengths and Difficulties Questionnaire: a research note. *J. Child Psychol. Psychiatry* 38(5), 581–586 (1997).

69 Beck JS, Beck AT, Jolly JB, Steer R. *Beck Youth Inventories of Emotional and Social Impairment (2nd Edition).* The Psychological Corporation, TX, USA (2008).