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Anxiety and depression in juvenile diabetes: A critical review

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Abstract

A critical examination of the recent literature on anxiety and depression in juvenile diabetes is presented. The objectives of this review are: (1) to determine the general association of psychological factors, especially anxiety and depression, with diabetes, (2) to examine the specific association of anxiety and depression with metabolic control, and (3) to propose methodological changes that are needed to advance future research in this field. The major conclusions of this review support the notion of a general association of psychological disorders with juvenile diabetes. However, while anxiety and depression appear to play an important and complex role in determining adaptation to the disease, their relationship to metabolic control does not yet appear clear. Additional prospective and controlled studies as well as multivariate models of chronic disease are now necessary to more fully understand the etiology and impact of these disorders in the adolescent population.

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1. Introduction

Insulin-dependent diabetes mellitus (IDDM) is a lifelong metabolic disorder requiring a complex treatment regimen of diet, exercise, and insulin by injection to achieve a normal

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metabolic state. Although current treatments have greatly improved the health status of people with IDDM, this condition remains associated with significant morbidity and mortality. IDDM is also the third most common chronic condition in young people under 16 years, after asthma and cerebral palsy (Betts, Buckley, Davies, McEvelly, & Swift, 1996). In light of its high prevalence and severity, it is not surprising that this condition has become the subject of considerable research from diverse clinical and scientific domains.

Several reviews of the literature have been published over the last 20 years concerning association of psychological disorders and IDDM. One of the earliest of these publications, a review of brittle diabetes (Greydanus & Hofmann, 1979), concluded that psychological factors appear to influence the course of diabetes mellitus, including metabolic control and the general management of the disease. Subsequent reviews have also underscored complexity of IDDM and the need to take into account patient variables, environmental factors, physiology, the role of stress, and the effects on health status into multifactorial models (Bennett Johnson, 1988). Among the most comprehensive reviews to date, Helz and Templeton (1990) examined the role of psychological factors in precipitating diabetes or in affecting its course from six different perspectives: anecdotal case reports, epidemiologic studies, clinical studies of discordant twin pairs, physiological effects of artificially induced stress, psychosocial interventions, and basic science investigations of responses to stress in humans and animals. These authors noted that psychological factors appear to play a very important role in diabetic control, a conclusion that is supported by other summaries of the literature showing that stress is reliably associated with changes in glucose regulation for a subset of diabetic patients (Beardsley & Goldstein, 1993). The most recent published review continues to observe greater psychiatric morbidity in IDDM patients than in the general population, with depression being the most common psychiatric disturbance followed by anxiety, and to indicate that these disorders have a direct impact on metabolic control (Eiber, Berlin, Grimaldi, & Bisserbe, 1997).

Despite these relatively consistent conclusions, past reviews have not been able to focus on the adolescent population. Adolescence is a time of rapid physical, psychological, and social change, and chronic illness has the potential to significantly influence this process of maturation and the transition of this population into adulthood (see Bussing & Aro, 1996). Such disorders can also disrupt normal family functioning, and adolescents with chronic diseases have generally been found to be at increased risk for depression, anxiety, and low self-esteem (Bennett, 1994; Kellerman, Zeltzer, Ellenberg, Dash, & Rigler, 1980; Magen, 1990; Seigel, Golden, Gough, Lashley, & Sacker, 1990; Suris, Parera, & Puig, 1996; Zeltzer, Kellerman, Ellenberg, Dash, & Rigler, 1980). While not all forms of chronic disease have been examined in detail in young populations, a considerable knowledge base has recently accumulated concerning the role of psychological factors in the course and outcome of diabetes. In light of this growing literature, the goals of the present article are: (1) to determine the relationship of anxiety and depression in juvenile diabetes; (2) to examine the association of anxiety and depression specifically with metabolic control; and (3) to propose the methodological changes that are needed to advance future research in this field. The selection of articles used in the current review was based on English and French language

investigations published over the last 10 years as identified through both Medline and PsychInfo databases.

2. Psychological factors and diabetes in children and adolescents

Since the last comprehensive review of the literature on psychological disorders in IDDM (Helz & Templeton, 1990), eight empirical investigations of adolescents samples have examined the association of anxiety and depression to this disease in terms of prevalence. Table 1 summarizes the results of these studies as well as their principal methodological characteristics.

Concerning retrospective and cross-sectional studies, a controlled investigation by Blanz, Rensch-Riemann, Fritz-Sigmund, and Schmidt (1993) found a significant association between psychological disorders and diabetes. Using a semi-structured interview, these authors found a prevalence of psychological disorders of 33.3% in the diabetic group compared with 9.7% in the control group. No specific behavioral profile was found for the diabetic adolescents except that they suffered from significantly more internalizing symptoms than their healthy counterparts, especially somatic symptoms, sleeping disturbance, compulsions, and depressed mood. Similarly, an uncontrolled study by Maronian et al. (1999) on 175 patients aged 2 to 25 years showed that 58.2% of the sample had at least one DSM-IV disorder, and particularly a high prevalence of anxiety disorders (19%) and eating disorders (18%).

In considering the prospective studies noted in Table 1, four of six investigations found a significant association of psychological disorders and IDDM. Grey, Cameron, Lipman, and Thurber (1995) studied the pattern of adjustment over 2 years in a cohort of 89 newly diagnosed diabetic children compared with a cohort of 53 peer-selected children without diabetes. They evaluated depression and anxiety by using self-report questionnaires and found that children with diabetes scored higher on the depression scale than the noncases at baseline and at 2 years postdiagnosis. Kovacs, Ho, and Pollock (1995) studied psychological disorders in ninety-two 8- to 13-year-old IDDM adolescent patients and found that the most common diagnosis in this population was adjustment disorder (36%), followed by the combination of adjustment disorder with depressed mood (18%). The risk factors for recovery from adjustment disorder were preexisting psychiatric disorder, parent marital distress, and maternal concern regarding the diabetes. However, the occurrence of a new disorder episode was independent from preexisting psychiatric morbidity. Kovacs, Goldston, Obrosky, and Bonar (1997) subsequently determined prevalence rates and risk factors for psychiatric disorders subsequent to the diagnosis of IDDM in adolescents by using semi-structured interviews repeatedly over a period of 10 years. Over 40% of the sample developed at least one episode of psychiatric disorder during the follow-up, 26% had major depressive or dysthymic disorder, nearly 20% developed some type of anxiety disorder, and 16% had behavior disorders. Concerning risk factors, only general maternal psychopathology emerged as a significant risk factor for psychiatric disorders in the IDDM patient.

Table 1
Relationship of diabetes to psychological disorders or problems in adolescents

Investigation	Design	Psychological assessment	Summary of results
Blanz et al., 1993	Cross-sectional, case-controlled: 93 cases (17–19), 93 noncases (healthy subjects)	Semi-structured interview (DSM-III-R)	Significant association: Rates of psychiatric disorders (33.3%) were significantly higher in the diabetic group more than threefold higher than in the control group (9.7%). The only significant difference between the two groups was the score for anxiety and depressive syndromes.
Kovacs et al., 1995	Prospective, noncontrolled (5 years): 92 cases (8–13).	Semi-structured interview (DSM-III)	Significant association: 33 Children developed adjustment disorder and 5 developed other psychiatric disorder in response to the diagnostic of IDDM.
Kovacs, Goldston, Obrosky, & Bonar, 1997	Prospective, noncontrolled (10 years): 92 cases (8–13)	Semi-structured interview (DSM-III), maternal psychopathology (SC90, BDI, HAM-D)	Significant association: By the 10th year of diabetes, an estimated 47.6% of the sample developed psychiatric disorder. Major depression had a significantly higher estimated prevalence (27.5%) than other disorders. The highest incidence rates were during the first year of the medical condition.
Grey et al., 1995	Prospective, case-controlled (24 months): 89 cases (8–14), 53 noncases (healthy peer)	Questionnaires: CDI, STAIC	Significant association: Children with diabetes scored higher on the CDI than the noncases initially and at 2 years postdiagnosis, but not at 1 year postdiagnosis.
Kovacs, Goldston, Obrosky, & Drash, 1997	Prospective, case-controlled (10 years): 24 cases, 30 noncases (depressed psychiatric subjects)	Semi-structured interview (DSM-III)	Significant association: Based on the same cohort as Kovacs, Goldston, Obrosky, and Bonar (1997), high rates of depression were observed in IDDM adolescents. However, overall rates of recovery and recurrence from major depressive disorder were indistinguishable in the diabetic and psychiatric control groups. Diabetic subjects were less likely to have had extended periods of time free of depression than controls.

Table 1 (continued)

Investigation	Design	Psychological assessment	Summary of results
Maronian et al., 1999	Retrospective study (3 years), noncontrolled: 175 cases (2–25)	Clinical interviews (DSM-IV)	Significant association: 102 Patients (58.2%) had at least one DSM-IV disorder. The main disorders were anxiety disorders (19%) and eating disorders (18%).
Northam et al., 1996	Prospective: 106 cases (1–14)	Questionnaires: CBCL, GHQ	Mixed association: At the first assessment, significantly more of the children 4 to 11 years old scored within the clinical range on internalizing disorders and total behavior problems. These differences were no longer significant 1 year later.
Jacobson et al., 1997	Prospective, case-controlled (10 years): 57 cases (19–26), 54 noncases (moderately severe, acute illness)	SCL-90R	No association: The level of reported psychiatric symptoms in the IDDM group did not differ from those of the comparison group at 10-year follow-up

CDI: Child Depression Inventory; STAIC: State Trait Anxiety Inventory for Children; CBCL: Child Behavior Checklist; SCL-90R: Symptom Checklist (revised); SC90: Symptom Checklist; BDI: Beck Depression Inventory; HAM-D: Hamilton Depression Rating Scale; GHQ: General Health Questionnaire.

Kovacs, Goldston, Obrosky, and Drash (1997) also studied whether IDDM affects the course of major depressive disorder in youth. It is important to underscore that the prevalence rates of major depression in this study are essentially the same as Kovacs, Goldston, Obrosky, and Bonar (1997), as these investigations utilized the same sample, but the former attempted to more clearly understand the role of IDDM in the course of this disorder. When these IDDM patients were compared with 30 depressed psychiatric controls, recovery from the first episode and the overall risk of a second episode did not appear to be associated with having IDDM. It is notable, however, that diabetic subjects were less likely to have had extended periods of time free of depression than psychiatric controls. Furthermore, gender was a risk factor in IDDM patients in that diabetic girls had 8.46 times the risk of a second episode as compared with boys, a finding consistent with epidemiologic data on gender differences in depression (albeit of lesser magnitude; Kessler et al., 1994).

Moreover, a prospective noncontrolled study on 103 children and adolescents aged less than 15 years examined the child and parents response to the diagnosis of diabetes with symptoms of psychological distress and dysfunctional family functioning (Northam, Anderson, Adler, Werther, & Warne, 1996) at a 1-year follow-up. The results showed mixed results in the sense that at first assessment, significantly more of the children 4 to 11 years scored within the clinical range on internalizing, and total behavior problems measured by the Child Behavior Checklist (filled by parents), but these differences were no longer significant 1 year later.

Finally, one prospective case-controlled study did not find any association between psychological disorders and IDDM. This investigation was based on a 10-year follow-up of patients aged 9 to 16 years at inclusion time. Data at inclusion time and at 10-year follow-up showed that there was no difference between the level of reported psychiatric symptoms in the IDDM group compared with the acute illness group (fractures, infection, appendicitis, lacerations, and other injuries; [Jacobson et al., 1997](#)). However, IDDM patients nonetheless reported lower perceived competence, with specific differences concerning evaluations of global self-worth, sociability, physical appearance, being an adequate provider, and humor. This mixed result and lack of association of the last investigation may be due to the choice of the acute illness group as a control group, since these children and adolescents at that time experienced a high stress level due to the acute illnesses. Therefore, the level of reported symptoms could be higher than without acute illness and diminished the difference with the diabetic group. Another reason could be that self-reported diabetes adjustment (assessed in terms of attitudes and feelings about diabetes) appeared to have improved at 10-year follow-up. Such findings may indicate adaptation to the disease, as some authors have shown that onset of diabetes would be associated with psychological symptoms that would lessen but not disappear in the 12 months following diagnosis ([Northam et al., 1996](#)).

3. Anxiety and depression in relation to metabolic control in children and adolescents

[Table 2](#) presents the eight studies since 1990 that have examined the association of psychological factors with metabolic control (as measured by the percentage of glycosylated hemoglobin in blood, HbA1c) as well as their possible interaction. Glycosylated hemoglobin, as measured by HbA1c, is one of the most commonly used indices of metabolic control in investigations on diabetes, reflecting the average level of blood glucose for the 3-month period before the day on which the sample was taken.

Only two of the eight studies found a significant association between depression and metabolic control ([Lernmark, Persson, Fisher, & Rydelius, 1999](#); [Maronian et al., 1999](#)). [Lernmark et al. \(1999\)](#), in a cross-sectional and uncontrolled study, compared a depressed diabetic group to a nondepressed diabetic group using self-report questionnaires. They found a significant difference when comparing means of metabolic control (although depression was not significantly associated with metabolic control when using multiple linear regression). Similarly, in a retrospective study, [Maronian et al. \(1999\)](#) found that diabetic children and adolescents with mental disorders, diagnosed by clinical interview based on DSM-IV criteria, had a poorer metabolic control than other diabetic patients at the first psychiatric consultation and 1 year later. These authors found that affective disorders, disruptive behavior disorders, and eating disorders were significantly associated with poorer metabolic control (measured by higher mean HbA1c), although there was a trend for patients with affective disorders and disruptive behavior disorders to improve their HbA1c status 1 year later. However, patients with and without anxiety disorders did not have significantly different HbA1c levels.

Table 2

Influence of psychological disorders or problems on metabolic control in adolescents

Investigation	Design	Psychological assessment	Summary of results
Kuttner et al., 1990	Cross-sectional, noncontrolled: 50 cases (10–16 years of at least one year diabetes duration)	Questionnaire: CDI	No association: No significant correlation between depression and HbA1c but attributional style for negative events and adherence measures explained 29% of the variance of HbA1c over the past year.
Grey et al., 1991	Cross-sectional, noncontrolled: 103 cases (8–18)	Questionnaires: STAI, CDI	No association: No significant association between anxiety and depression with metabolic control. Poorer metabolic control was associated with several of the coping behaviors such as investing in close friends ($r=.25$, $P<.01$), avoidance behaviors ($r=.31$, $P<.01$), and daydreaming ($r=.23$, $P<.01$).
Rothbaum et al., 1992	Cross-sectional, noncontrolled: 34 cases (7–18)	Questionnaire: CDI	No association: No correlations between HbA1c and self-concept, positive mood or depression. However HbA1c prior to assessment was positively correlated with number of symptoms at assessment time ($r=.47$, $P<.005$) and HbA1c at assessment time was correlated with negative mood ($r=.35$, $P<.04$).
Lernmark et al., 1996	Cross-sectional, noncontrolled: 56 cases (<15 years)	Questionnaire: Koppitz's scale (emotional indicators)	No association: None of the psychological and psychiatric variables were related to mean HbA1c levels up to 24 months after disease onset. Boys with more hospitalizations had a more external locus of control ($r=.52$, $P=.01$). Boys reporting more difficulties with adjustment to the disease showed more emotional problems with the Koppitz assessment ($r=.71$, $P=.001$) and were also clinically assessed as having more problems ($r=.47$, $P=.05$).
Lernmark et al., 1999	Cross-sectional, noncontrolled: 62 cases (9–18)	Questionnaires: CDI Fear Survey Schedule	Significant association: Compared to a nondepressed group, depressed patients showed significant differences in metabolic control ($P<.01$), adaptation ($P<.001$), and self-esteem ($P<.001$). Adaptation was the only significant variable to predict metabolic control in regression analyses (17% of the variance). When studying the adaptation subscales, "monitoring" explained 26% of the variance in HbA1c ($P<.0001$).

(continued on next page)

Table 2 (continued)

Investigation	Design	Psychological assessment	Summary of results
Blanz et al., 1993	Cross-sectional, case-controlled: 93 cases (17–19), 93 noncases	Semi-structured interview (DSM-III-R)	No association: No significant correlation was found between the severity of psychiatric disorders and metabolic control, including when comparing psychiatric disorders in the three metabolic groups (good, moderate, and bad).
Kovacs et al., 1996	Prospective (9 years), noncontrolled: 88 cases (8–13 years with new-onset diabetes)	Semi-structured interview (DSM-III)	No association: When psychiatric diagnoses were partitioned into depressive and nondepressive disorders, the data failed to support that depression has a deleterious effect on HbA1. The final model of repeatedly assessed HbA1 levels suggests that noncompliance with medical treatment and the interaction of nondepressive psychiatric disorder with time contribute to moderate worsened metabolic control.
Maronian et al., 1999	Retrospective study (3 years): 175 cases (mean age 13.5 years)	Clinical interviews (DSM-IV)	Significant association: Affective disorders, disruptive behavior disorders, and eating disorders were significantly associated with a poor metabolic control. But patients with and without anxiety disorders did not have significantly different HbA1c levels.

CDI: Child Depression Inventory; STAIC: State Trait Anxiety Inventory for Children; CBCL: Child Behavior Checklist; SCL-90R: Symptom Checklist (revised); SC90: Symptom Checklist; BDI: Beck Depression Inventory; HAM-D: Hamilton Depression Rating Scale.

In contrast to these two investigations, six recent studies found no association between anxiety or depression and metabolic control (Blanz et al., 1993; Grey, Cameron, & Thurber, 1991; Kovacs, Mukerji, Iyengar, & Drash, 1996; Kuttner, Delamater, & Santiago, 1990; Lernmark et al., 1996; Rothbaum, Salas, & Heiss, 1992). In an investigation by Kuttner et al. (1990) on 50 IDDM adolescents aged 10 to 16 years, a significant association was found only between learned helplessness (not depression) and worsened metabolic control over the preceding year. Specifically, the role of helpless attributional style was linked to the mean of HbA1 scores over the preceding year and to current HbA1 regimen adherence. These authors suggested that learned helplessness is associated with metabolic control via regimen adherence. Another study of 103 adolescents aged 8 to 18 focused on the influence of age, coping behaviors, and self-care on psychological, social and physiologic adaptation (Grey et al., 1991). Taking into account adolescent maturity, it was found that poorer metabolic control was associated with several coping behaviors such as investing in close friends, avoidance behaviors, and daydreaming. Based on these results, the authors concluded support for a model of developmental differences in response to diabetes. However, no association was found between anxiety and depression and metabolic control. Furthermore, the lack of a

control group did not allow the authors to conclude that coping behaviors could be due more to the presence of the disease than to developmental stages.

Rothbaum et al. (1992) studied psychological aspects linked to physical health in 34 diabetic children and adolescents aged 7 to 18 years. Again, no significant association was found for metabolic control and self-concept, positive mood, or depression. However, metabolic control evaluated 3 months before assessment was positively correlated with several symptoms at assessment time, and metabolic control at assessment time was itself correlated with negative mood. This latter result suggests that complaints of specific symptoms could be more important to detect psychological problems than depression evaluated by self-administered questionnaires. Finally, a study by Lernmark et al. (1996) examined psychosocial factors in IDDM in the goal of improving psychosocial aspects of diabetes care. None of the psychological and psychiatric variables tested were found to be related to mean HbA1c levels up until 24 months after disease onset. In another recent study aimed at investigating the longitudinal relationship between psychiatric diagnostic variables and metabolic control among youths with IDDM, psychiatric morbidity and duration of IDDM were found to have an interactive effect on metabolic control, with IDDM duration being more salient than age in this regard (Kovacs et al., 1996).

Possible explanations for these discrepant results could be mostly due to the types of statistical analyses employed. For example, Lernmark et al. (1999) showed that when comparing a diabetic depressed group to a diabetic nondepressed group, means of metabolic control were indeed different. However, when using regression analyses, only adaptation predicted variance of metabolic control. When looking closer at the association among the variables, adaptation was related both to symptoms of depression and metabolic control, but depression itself could not explain variance of metabolic control. Similar statistical issues were present in the study by Marionan et al. (1999), who comparing diabetic groups on presence or absence of psychiatric disorders and found significant differences for affective and anxiety disorders. But when using regression analyses, only affective disorders, disruptive behavior disorders, and eating disorders explained variance of metabolic control.

These different findings underscore the likely role of third variables, and multicollinearity among variables, in attempts to explain metabolic control. Among the numerous additional predictors, three different studies also highlighted the role of medication adherence and management in the evolution of metabolic control (Kovacs et al., 1996; Kuttner et al., 1990; Lernmark et al., 1999). Kuttner et al. (1990) found that attributional style for negative life events and adherence to treatment plans explained 29% of the variance of HbA1 over the previous year. In a study on 62 children and adolescents aged 9–18 years old (with at least a 2-year history of type I diabetes), Lernmark et al. (1999) found that adaptation, and in particular monitoring, explained 26% of the variance in HbA1. Moreover, Kovacs et al. (1996) found that noncompliance with medical treatment and the presence of a nondepressive psychiatric disorder contributed to moderately worsened metabolic control over time. Other risk factors were also found to moderate metabolic control including coping behaviors such as investment in close friends, avoidance behaviors, and daydreaming (Grey et al., 1991), locus of control (Lernmark et al., 1996), or somatic symptoms and negative mood (Rothbaum et al., 1992). Finally, a recent prospective investigation on the role of adverse life events in

glycaemic control found that glycated hemoglobin values at 12 months were significantly higher in children who had experienced one or more events than in children who had experienced no events (Worrall-Davies, Holland, Berg, & Goodyer, 1999). These additional variables can be related to metabolic control either directly or indirectly, but may also be precursors of anxiety and depression disorders. As such, anxiety and depression in juvenile diabetes may be conceptualized both as consequences of this chronic illness and as markers of maladjustment to the disease (inefficacy of coping strategies, specific personality traits such as learned helplessness. . .).

4. Summary of the recent literature, methodological critique

Concerning evidence for the role of psychological factors in diabetic children and adolescents, cross-sectional and prospective studies over the past decade provide generally consistent support for the presence of anxiety and depression in juvenile diabetes. Of the eight empirical studies selected, six found a significant association between psychological disorders and diabetes (Blanz et al., 1993; Grey et al., 1995; Kovacs, Goldston, Obrosky, & Bonar, 1997; Kovacs, Goldston, Obrosky, & Drash, 1997; Kovacs et al., 1995; Maronian et al., 1999), whereas one found mixed results (Northam et al., 1996) and one no association (Jacobson et al., 1997). However, of eight studies published since 1990 focusing on the links between anxiety, depression, and metabolic control, only two studies found a significant association of anxiety and depression with metabolic control (despite other significant associations reported for life events, treatment compliance, perception of control, and specific coping behaviors). It is important to note that these conclusions reflect findings reported across investigations that vary considerably concerning diverse methodological details including study design, sample source and control group characteristics, assessment techniques, and statistical analyses. The following paragraphs will present a discussion of these issues in terms of their influence on the present conclusions as well as changes necessary to improve future investigations and clinical implications of these results.

Concerning basic study design issues, cross-sectional and retrospective studies represent significant portion of the studies presented in this review. While such approaches can demonstrate a basic association between variables, they cannot determine the direction of these relationships. For example, the few studies to find a significant association between anxiety and depression and metabolic control when comparing depressed with nondepressed diabetic patients are unable to elucidate the potentially causal associations among these conditions (e.g., Lernmark et al., 1999). In this respect, future research particularly concerning metabolic control must integrate prospective assessments of both anxiety and depression (as well as repeated assessments of metabolic control) to determine the nature of this relationship.

A second important issue concerns the sociodemographic characteristics of the sample studied, and in particular, the variables of age and sex. In most of the studies selected, the samples were composed of a wide range of children and adolescents aged from 7 to 18 years old, a fact which represents a potential bias as diabetes and metabolic control appear to be age and sex dependent (Grey et al., 1991). For example, some authors found that boys had better

metabolic control than girls, and that there is generally a negative correlation between metabolic control and the age of the child or the duration of diabetes (Kaar, Akerblom, Huttunen, Knip, & Sakkinen, 1984). While some investigations have reported that HbA1c levels have no relation to puberty stage (e.g., Zachrisson, Wallensteen, & Dahlquist, 1995), the most recent studies continue to conclude support for such an association (Thomsett, Shield, Batch, & Cotterill, 1999). Aside from this enduring debate, demographic factors also appear important for other reasons in interpreting the research on anxiety and depression in the adolescent IDDM population. For example, studies have shown that depressed subjects have different symptoms as a function of both age (Cohen et al., 1993) and gender (Hankin & Abramson, 1999; Wichstrom, 1999). Still other research has underscored the interaction of these demographic variables in that the emerging gender difference for depression (with more girls being depressed than boys) generally appears after the age of 13 years (Hankin & Abramson, 1999; Wichstrom, 1999). In light of these observations, studies of depression, anxiety, and metabolic control should include patients of similar age, for example, preadolescents or adolescents only, or to control statistically for such variation, in order to have the most homogeneous sample as possible.

The use of a control group is a third major methodological concern, as its integration in clinical research is essential for yielding estimates of relative risk. However, of the 13 studies selected for the present review, only four used a control group. Concerning metabolic control, three of these four found no significant association with psychiatric disorders (Blanz et al., 1993; Jacobson et al., 1997; Kovacs, Goldston, Obrosky, & Bonar, 1997; Kovacs, Goldston, Obrosky, & Drash, 1997). It is important to note, however, that the choice of control group characteristics may lead to false conclusions, as one of the cited studies used a psychiatric control group (Kovacs, Goldston, Obrosky, & Bonar, 1997; Kovacs, Goldston, Obrosky, & Drash, 1997) and one used an acute illness control group (Jacobson et al., 1997). Thus, the lack of associations reported by these studies may be due to the fact that choosing such control groups (affected by other conditions) could reduce normally observable differences on measures of anxiety and depression. By contrast, however, if the goal of the study is to understand the association of anxiety and depression *specifically* with diabetes (rather than with a chronic disease), a more informative way to study these relations would be to use subjects having other chronic illnesses as the comparison group as the increased prevalence of psychological disorders in diabetic population may reflect a generic effect of increased stress due to having a chronic medical condition (see Jacobson, 1993). This approach should therefore identify factors associated with IDDM separately from those associated with most chronic diseases (Stein & Jessop, 1982). Although a comparative choice has been used in few studies (e.g., Esparbes-Pistre, 1997), it is likely that an appropriate group in research on diabetes would be to choose subjects with another frequent chronic disease such as asthma. This latter chronic disease has much in common with diabetes in terms of management and compliance (daily intake of medication, crisis management, and regular visits to the general practitioner) and is characterized by a relatively high population prevalence which should reduce biases associated with the study of rare disorders (such as social stigma, or lack of public knowledge). A meta-analysis of depressive symptoms among children and

adolescents with chronic medical problems (Bennett, 1994) showed that children with certain disorders (asthma, recurrent abdominal pain, sickle cell anemia) may be at greater risk than children with other disorders (cancer, cystic fibrosis, diabetes mellitus). In this respect, the association anxiety and depression with diabetes should be understood not only in terms of healthy controls but also relative to other chronic diseases.

A fourth methodological issue concerns variance in questionnaires or semi-structured interviews used to evaluate psychological disorders. Perhaps due to feasibility issues, the use of self-report questionnaires for the assessment of anxiety and depression is more often in cross-sectional than in prospective studies. Nonetheless, validity problems have been reported concerning the use of these questionnaires and such issues may influence the confidence one may have in past studies. For example, Canning and Kelleher (1994) examined the sensitivity, specificity, and positive or negative predictive values of three different screening questionnaires for emotional and behavioral disorders in chronically ill children and adolescents (diagnosed with cancer, cystic fibrosis, inflammatory bowel disease, and IDDM). These scales were compared with the diagnoses obtained by an intensive structured psychiatric interview (Diagnostic Interview Schedule for Children). The questionnaires demonstrated low sensitivity, low positive predictive value, and low negative predictive value, but high specificity. The authors concluded that they should not be relied on as screening instruments for psychopathology in children and adolescents with chronic medical conditions. The major source of problems appeared to be due to the somatic items of the scales, in that chronic diseases (and particularly diabetes) can influence the responses to such questions. It therefore seems necessary to first make a direct psychiatric diagnosis based on clinical interview when possible, or to only use questionnaires specifically validated on the population studied.

Finally, an important source of variance in the reviewed studies concerns the way in which the relationship between diabetes and anxiety or depression has been analyzed. For example, Lernmark et al. (1999) conducted intergroup comparisons in a juvenile diabetic sample. They found differences on depressive disorders only when comparing a depressed and a nondepressed group means, but when explaining metabolic control in multiple regressions, no significant role was found for depression. A logistic or linear regression takes into account other independent variables that could interfere in the relationship between the dependent variable and the numerous predictors under study (see Falissard, 1996), therefore providing more conservative estimates for the role of specific constructs. Future research should benefit from applying similar or additional sophisticated analytic techniques (including latent class or multilevel models) that should clarify the major sources of variance among diverse associated predictors.

In summary, there is now considerable evidence in support of an association between psychological disorders such as anxiety or depression and juvenile diabetes. However, the relationship of these variables to metabolic control does not appear strong. Attention to the previously noted methodological issues should reduce differences across investigations and clarify these basic findings in the years to come. Investigations are needed that will focus on the adolescent diabetic population using a biopsychosocial clinical model of the disease, and that take into account additional psychological variables that may play an indirect role in

metabolic control. Prospective and controlled studies using multivariate models are also necessary to adequately study these diverse factors and to advance future research in this field. Finally, the clinical implications for these results are important to consider and they emphasize the need for health professionals to systematically screen diabetic adolescents for anxiety and depression. As these disorders can have an important impact on quality of life of patients with juvenile diabetes, psychosocial interventions should be proposed when needed as well as patient and family education concerning treatment adherence and control of the disease.

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