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Type 1 diabetes is associated with alexithymia in nondepressed, non-mentally ill diabetic patients: A case-control study

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Abstract

Objective: Alexithymia refers to difficulty in identifying and expressing emotions, and it is a characteristic common to several psychiatric and medical conditions, including autoimmune disorders. Type 1 diabetes (T1D) is an autoimmune disorder with increased psychiatric comorbidity. Previously reported associations between alexithymia and T1D may have been confounded by the presence of depression. The central aim of this study was to examine alexithymia levels in psychiatrically uncomplicated T1D outpatients with that of nondiabetic controls. **Methods:** Ninety-six T1D patients without any *DSM-IV* Axis I diagnoses and 105 age- and sex-matched healthy controls entered the study. Alexithymia and depressive symptoms were assessed with the Toronto Alexithymia Scale (TAS-20) and the Beck Depression Inventory (BDI-21), respectively. Multivariate regression models were used to evaluate the association of alexithymia with the presence of diabetes, duration of diabetes, diabetes control, parameters of treatment intensification, and diabetic complications. **Results:** T1D was positively associated with the TAS-20 "identifying feelings" (β coefficient=2.64, P=.003) and "externally oriented thinking" (β coefficient=1.73, P=.011) subscales. The prevalence of overall alexithymia (TAS-20 total score, ≥60) was 22.2% in T1D patients and 7.6% in the controls (OR, 4.6; 95% CI, 1.7–12.8). TAS-20 scores were positively associated with diabetes duration and negatively with treatment intensification parameters. **Conclusions:** Alexithymia is higher in psychiatrically uncomplicated T1D patients than in healthy controls even after adjustment for confounding depressive symptoms; it is greater with longer diabetes duration and is associated with some reduced parameters of treatment intensification but not with worse outcome in terms of glycemic control or somatic complications.

Keywords: Alexithymia; Type 1 diabetes; Depression; Case-control study

Introduction

Type 1 diabetes (T1D) has long been identified as a disease with increased psychiatric comorbidity such as anxiety and depression [1,2]. In the face of a complex, demanding, and often confusing set of self-care directives, patients may become frustrated, angry, overwhelmed, and/or discouraged while they have to cope with life-threatening risk of metabolic dyscontrol, conflicts with family, and the potential strained relationships with health care providers [3].

Alexithymia [4,5] is viewed as a dimensional personality construct that encompasses a cluster of cognitive and affective characteristics relating to a deficiency in identifying and describing emotions, externally oriented thinking style, and limited imaginal capacity, resulting in deficient self-regulation of affective responses and dissociation of emotional and physical responses to life events and bodily sensations [6–10]. These alexithymic characteristics are thought to contribute to the onset or maintenance of several

Abbreviations: BDI, Beck Depression Inventory; TAS-20, Toronto Alexithymia Scale; T1D, Type 1 diabetes.

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psychosomatic, medical, and psychiatric disorders [6], as a risk factor for these disorders [6,11,12], but equally, trauma, stress, or even health problems during adolescence or adulthood can trigger alexithymia [12], so-called secondary alexithymia [13,14]. Although alexithymia has also been viewed as a defense mechanism that protects chronically ill patients from stress and its consequences [15], it is predominantly considered a deficit rather than a defensive process [12] and this deficit view is gaining increasing support from basic laboratory research [16–19].

There are few studies that examined the association between alexithymia and T1D [20–23], and only two compared the prevalence of alexithymia in diabetic patients with that of a control group [20,23], while no study excluded diabetic subjects diagnosed with clinical depression or other psychiatric disorders. The latter may be prevalent in diabetes [1,2] and is associated with alexithymia [21,24–26]. The aim of the present case-control study was to measure the levels and prevalence of alexithymia and perceived depression in T1D outpatients who did not meet the criteria for major depression or any other psychiatric diagnosis. A secondary goal was to examine whether alexithymia was associated with duration of T1D, parameters of treatment intensification, glycemic control, and diabetic complications.

Methods

Participants

The study was approved by the Venizelion Hospital Ethics Committee. All T1D outpatients followed up for at least 1 year in the Diabetic Clinic of Venizelion General Hospital in Heraklion, Greece (N=110), were asked to participate in the study. One hundred and six patients (96%) agreed to participate. Inclusion criteria were age 18–60 years and written informed consent, while exclusion criteria were (i) blindness (one subject); (ii) end-stage renal disease (one subject); (iii) nonfluent in written and spoken Greek language (none); (iv) any *DSM-IV* Axis I disorder currently or in the last 12 months, based on a Structured Clinical Interview for DSM-IV Axis I Disorders [27]. Ninety-six T1D patients met these criteria and entered the study. One hundred and five sex- and age-matched (within a 5-year window) healthy controls without a previous history of diabetes and/or depression were recruited, based on medical records and a Mini-International Neuropsychiatric Interview [28]. They were identified from lists of employees living in the same town of Heraklion and were selected from nurses and office workers of the university hospital and from postal clerks at the central office of the town.

Diabetes characteristics—complications of disease

The medical data collected by three diabetologists (IC, EK, MS) included information on duration of type 1 diabetes (years since diagnosis), number of glucose measurements per week, number of insulin injections per day, number of mild hypoglycemias during the past week, number of severe hypoglycemias that required hospitalization during the past year, and medical history of coronary heart disease. Diabetic retinopathy was established with retinal examination using an indirect ophthalmoscope following pupil dilatation and/or fluoroangiography if necessary. Diabetic nephropathy was determined by micro- or macroalbuminuria. HbA_{1c} measurement was performed with a Bayer DCA2000 Analyzer, a model that is certified by the USA National Glycohemoglobin Standardization Program for its comparability to the reference methods established by the Diabetes Control and Complication Trial [29].

Instruments

All participants were asked to answer a questionnaire on sociodemographic characteristics: age, education level (years of education), socioeconomic background (using the UK Registrar General's 1990 classification according to occupation by ISCO88 code), marital status, weight and height (self-reported), and smoking status (current smoker/ex-smoker/never smoker).

Toronto-Alexithymia Scale

Alexithymia was assessed with a validated Greek translation of the 20-item Toronto Alexithymia Scale (TAS-20), comprising three factors: difficulties identifying feelings, difficulties expressing feelings, and externally oriented thinking, each yielding a subscale score [30,31]. In the Greek TAS confirmatory factor analysis study, the three factor scores revealed no significant differences between the normal adults and asthmatic patients [30]. TAS-20 has been the most widely used measure in alexithymia research, and a wealth of data have been accumulated supporting its validity to predict both basic emotional processes and clinical criteria [12,31]. Items consist of statements presented in a five-point Likert scale (score, 1–5) along a *strongly disagree* to *strongly agree* continuum, with higher scores indicating more alexithymia.

Beck Depression Inventory

All participants were asked to fill in the Beck Depression Inventory, 21-item version (BDI-21), a widely used and well-validated self-report inventory of depressive symptoms [32].

Statistical analysis

The statistical software SPSS 15.0 (SPSS, Inc., Chicago, IL, USA) was used for the analysis. Univariable analysis of categorical variables was made using the Pearson chi-square test. Continuous variables were presented as means and standard deviations (S.D.), and univariable analysis was made using both parametric (independent samples t test) and nonparametric (Mann–Whitney) tests, as appropriate. TAS-20 total scores were used dimensionally (score range,

20–100) or categorically, indicating yes or no alexithymia (score, ≥60 and <60, respectively) [33]. BDI-21 scores were used either as a continuous (score range, 0–63) or a categorical variable with a cut-off point of 14/15 to categorize the study subjects with self-reported depression (total score, ≥15) or nondepression (total score, ≤14) [34].

Multivariable linear regression models were performed to evaluate the association of TAS-20 subscale scores with the presence of diabetes (duration of diabetes, age of onset), diabetes control (HbA_{1c}, number of mild or severe hypoglycemia in the last year), parameters of treatment intensification (number of glucose measurements/week, number of insulin injections/day), and diabetic complications (retinopathy, coronary heart disease, nephropathy). In addition, we performed a sensitivity analysis using TAS-20 total score as a categorical variable (multivariate logistic regression). The following variables were considered as potential confounding factors: age, sex, BMI, education, smoking status, and perceived depression (BDI-21 scores). All hypothesis testing was conducted assuming a .05 significance level and a two-sided alternative hypothesis.

Results

Table 1 describes the sociodemographic characteristics of T1D patients and controls and the clinical profile of the T1D patients. Cases and controls did not differ significantly in terms of BMI, smoking, and marital status, whereas the T1D patients had lower educational level than controls (P=.023).

Mean (±S.D.) TAS-20 total and subscales scores were 48.3±11.9 (subscales: "identifying feelings," 16.9±6.4; "expressing feelings," 11.8±4.4; and "externally oriented thinking," 19.5±4.7) for the patients and 41.6±10.9 (subscales: "identifying feelings," 13.4±6.1; "expressing feelings," 10.9±4.0; and "externally oriented thinking," 17.3±4.6) for the controls. Table 2 presents the full findings of the final linear regression models for the three TAS subscales, including as potential confounders only those variables which related with the outcome of interest in the bivariate models with a P value of <.2 (i.e., education and BDI-21 score). T1D was positively associated with the "identifying feelings" and "externally oriented thinking" subscales. Identical results were obtained when age, sex, BMI, and smoking status were included as additional potential confounders. The prevalence of overall alexithymia (TAS-20 total score, ≥60) was 22.2% in T1D patients and 7.6% in the controls (OR, 4.6; 95% CI, 1.7–12.8, after adjusting for the same confounders as in Table 2).

Mean (±S.D.) BDI-21 score was 8.5±11.9 in diabetic subjects and 7.6±10.9 in controls (β coefficient=0.52, P=.629). The prevalence of self-reported depression (BDI-21 score, ≥15) did not differ significantly between the two groups (16% in cases vs. 12.4% in the controls; P=.221). TAS-20 and BDI-21 scores were correlated significantly in T1D patients (r=0.265, P=.012) and controls (r=0.518, P<.001); therefore, we included BDI-21 score as an independent variable in the multivariate regression models.

Table 1
Sociodemographic characteristics of diabetic subjects and controls, and clinical profile of diabetic subjects

Demographic characteristics	Cases	Controls	P value *
Sex, n (%)			
Male	38 (39.6)	46 (43.8)	.616
Female	58 (60.4)	59 (56.2)	
Smoking status, n (%)			
Never smoker	44 (45.8)	45 (42.9)	.663
Ex smoker	16 (16.7)	21 (20.0)	
Current smoker	35 (36.5)	39 (37.1)	
Age, mean±S.D.	35.1±10.0	35.8±8.0	.412
BMI, mean±S.D.	25.4±4.0	25.4±4.3	.933
Years of education, mean±S.D.	12.7±2.7	13.9±1.6	.001
Diabetes characteristics, mean±S.D.			
Years since diagnosis	16.2±8.0	NA	NA
Last measurement HbA_{1c}	7.7±1.4	NA	NA
Mean HbA_{1c} (last three measurements)	7.9±1.4	NA	NA
Glucose measurements per week	18.9±14.4	NA	NA
Insulin injections per day	3.8±1.2	NA	NA
Hypoglycemias felt last week	2.2±2.2	NA	NA
Hospitalizations for hypoglycemia last year	0.1±0.6	NA	NA
Complication of diabetes, n (%)			
Diabetic retinopathy	25 (26)	NA	NA
Retinal photocoagulation	16 (16.7)		
Vitrectomy treated	1 (1)	NA	NA
Diabetic nephropathy	14 (14.6)		
Microalbuminuria	10 (10.4)		
Albuminuria	4 (4.2)		
Coronary heart disease	2 (2.1)	NA	NA
History of a heart infarct	1 (1)		
Coronary artery by pass surgery	1 (1)		

* Chi-square test was used for categorical variables; independent samples t test was used for continuous variables; NA: not applicable.

In the group of diabetic patients, duration of diabetes was associated with increased total TAS-20 score (β coefficient=0.25, P=.055) and, in particular, with the "identifying feelings" subscale at a trend level (β coefficient=0.14, P=.061) and the "externally oriented thinking" subscale (β coefficient=0.10, P=.047). On the other hand, alexithymia (total TAS-20 score) was inversely associated with some parameters of treatment intensification, indicating a trend level reduction of 0.16 for the number of glucose measurements per week (β coefficient=−0.16, P=.074) and 2.06 for the number of insulin injections per day (β coefficient=−2.06, P=.05). There were no associations between alexithymia and T1D age of onset (β coefficient=0.27, P=.09), number of hypoglycemias in the last year (β coefficient=0.88, P=.16), HbA_{1c} (β coefficient=−0.04, P=.97), or presence of somatic complications (β coefficient=4.78, P=.09).

Discussion

This is the first study to examine alexithymia in a nondepressed, but demographically and nosologically,

Table 2
Multivariable linear regression models of the determinants of TAS-20 subscale scores

	Unstandardized coefficients		Standardized coefficients			95% Confidence interval for *B*	
Model predictors	*B*	Standard error	*β*	*t*	Significance	*B*	Standard error
TAS-20 "Identifying feelings" subscale							
Years of education	−0.74	0.56	−0.10	1.33	.185	−1.84	0.36
Presence of type 1 diabetes [a]	2.64	0.88	0.17	2.38	.003	0.36	3.89
BDI-21 score [b]	0.33	0.06	0.37	5.44	.001	0.21	0.44
TAS-20 "Expressing feelings" subscale							
Years of education	−0.58	0.38	−0.12	1.54	.125	−1.32	0.16
Presence of type 1 diabetes	0.33	0.59	0.13	1.80	.583	−0.04	0.75
BDI-21 score [b]	0.19	0.04	0.34	4.72	.001	0.11	0.27
TAS-20 "Externally oriented thinking" subscale							
Years of education	−0.73	0.44	−0.13	1.67	.096	−1.59	0.13
Presence of type 1 diabetes	1.73	0.68	0.15	1.96	.011	−0.01	2.75
BDI-21 score [b]	0.04	0.05	0.07	0.96	.339	−0.05	0.14

[a] Reference category: healthy controls.
[b] BDI-21 score: Beck Depression Inventory score.

representative sample of T1D patients compared to healthy controls. Inclusion of alexithymia either as a dimensional or as a dichotomous variable in the analyses always showed higher levels or prevalence, respectively, of alexithymia in the T1D patients compared to healthy controls in the absence of depression or any other psychiatric disorder. We report lower prevalence of alexithymia in our T1D group compared to previous studies on T1D patients [23] or on T1D patients undergoing hemodialysis [35–37]. This may be because depression and other psychiatric diagnoses were excluded from our sample and the possibility that T1D undergoing hemodialysis may be at the more severe end of the spectrum with high psychiatric comorbidity. Alexithymia is a normally distributed personality trait with a prevalence varying from 7% to 13% in the general population [24,38,39], which is in accordance with its prevalence in our control group. Our results could not be attributed to differences in prevalence of BDI-21-defined depression, level of depressive symptomatology, or demographic variables since the two groups did not differ in this respect and the small difference in years of education was controlled for.

We found that alexithymia levels in psychiatrically uncomplicated T1D were associated with marginally fewer blood glucose measurements per week and fewer self-administered insulin injections per day. These findings are open to two contrasting interpretations: (a) reduced motivation or capacity for self-management in the most alexithymic patients. The most obvious implication here would be the need for enhanced support in T1D patients in the context of a multidisciplinary approach, given the role of compliance in the prognosis of metabolic control and the course of T1D [40–42]. However, this interpretation would be inconsistent with a previous report suggesting that alexithymia was unrelated to adherence in diabetes treatment [21]. Future research should include rigorous and quantified assessment of compliance in nondepressed T1D patients; (b) alternatively, it is possible that higher alexithymia in nondepressed/mentally ill T1D patients is associated with a more favorable course of the illness such that prescription of treatment intensification may be less required. It is interesting in this respect that alexithymia in T1D was not associated with glycemic control or diabetes complications, which is in contrast to previous reports [20,22,23]. This discrepancy may be due to the exclusion of T1D patients with depression and other psychiatric syndromes, in contrast to all previous studies. Depression may affect motivation and self-care (*DSM-IV*) [43] and is associated with reduced compliance, self-care, and glycemic control in T1D [40,41,44]. Indeed, alexithymia was found to be associated with depression, but alexithymia alone was unrelated to somatic variables in T1D [21], severity of chronic pain [45], or other serious medical conditions [46]. All the above taken together suggest that depression may be a confounder in studies of alexithymia levels in T1D or its effect on T1D outcome, and that depression more than alexithymia led to loss of glycemic control in previous studies which had not excluded depressed T1D patients.

The observation that alexithymia levels were greater with greater T1D duration could suggest that alexithymia develops post T1D diagnosis as a consequence of diabetes. Such secondary alexithymia has been previously shown to develop following trauma, stress, or health problems during adolescence or adulthood. Indeed, substantial elevation of alexithymia was found in Holocaust survivors [47], victims of sexual violence [48], patients with posttraumatic stress disorder [49–51], those who have suffered severe burns [52], and patients undergoing chronic and intrusive treatments such as hemodialysis [35–37] and after a head injury [53]. Secondary alexithymia has been related to the consequence of the distress associated with the psychiatric disorder [13]

and has been reported to be influenced by psychiatric states such as anxiety, depression, and anhedonia [54]. The frequently observed association between alexithymia and depression or anxiety has suggested a state-dependent phenomenon [25,55,56] whereby high alexithymia reflects current affect and situational variables that impose on one's cognitive/affective processing capacity. It is thus important that, compared to controls, we observed higher alexithymia in T1D patients who were free of psychiatric illnesses, especially depression. Our findings placed in the context of the general literature suggest that alexithymia, at least in T1D, may be a complex manifestation that includes both T1D-specific (trait) and state components. Future research should attempt to differentiate these by assessing premorbid or developmental functioning.

How does the presence of diabetes affect one's ability to identify and process one's emotions? Emotional processing depends normally on the activity of certain brain areas, the volume of which is reported to be reduced in alexithymic subjects [57]. It is interesting that hypoglycemic states in T1D activate areas of this network such as the amygdala and orbitofrontal cortex [58], which are key areas for the labeling and awareness of emotions [59,60], and that unawareness of hypoglycemia in T1D patients is associated with reduced activation of these areas [58]. There is evidence of dysfunction of this network in T1D; indeed, performance in neuropsychological tests, which depend on the integrity of anterior and medial temporal/frontal regions, reveals cognitive deficits as early as 2 years after diabetes onset [61,62]. It is possible that, in addition to the documented T1D-induced cognitive decline which could underlie the lower educational achievement in our T1D sample, T1D may also cause increasing difficulty in emotional processing. It is not known whether the above mechanisms would be specific to T1D, but it is interesting that the prevalence of alexithymia observed in the present study (22.2%) in T1D patients is comparable to that of patients with other autoimmune conditions such as 27.5% in rheumatoid arthritis [63]. It is also interesting in this context that in a Greek study comparable in terms of population size, no differences were found in any of the three TAS subscale scores between normal controls and patients suffering from asthma, a chronic but not an autoimmune condition [30]. More research is required to determine whether and how alexithymia is related to cognitive and emotional processing deficiencies in T1D patients using specific neuropsychological batteries and paradigms of emotional processing, e.g., startle modulation by affective pictures.

Strengths of this study include assessment of nondepressed diabetic patients and matched healthy controls, the use of validated self-reported questionnaires, and detailed medical history. However, several limitations should also be considered: First, the cross-sectional nature of the study does not allow the assessment of causal relationships. The patient sample was relatively small, although the low standardized annual incidence rate of T1D in Crete (6.1 per 100,000 persons for childhood type 1 diabetes) [64] should be taken into account. Second, the lack of a control group suffering from chronic somatic illness does not allow assessment of the specificity of our findings to T1D vs. chronicity of illness. In addition, our T1D sample was relatively inhomogeneous in terms of the clinical form of the illness (e.g., with and without somatic complications) and the number of predictors to cases may be suboptimal in the multiple regression analyses in this group. Finally, although we cannot entirely rule out biases from individual, social, and educational status, we have no indication from our data of differential selection bias in the study groups. Participants were unaware of the hypothesis being tested, so misclassification of exposure by questionnaires is likely to be random with respect to diabetes.

In conclusion, the present study suggests that, compared to healthy controls, the levels and prevalence of alexithymia are higher in nondepressed or otherwise mentally ill T1D patients, after controlling for confounders such as education and subjective depressive symptomatology. Higher alexithymia in the patient group was associated with greater T1D duration and some reduced parameters of treatment intensification but not with worse outcome in terms of glycemic control or somatic complications. More comprehensive and longitudinal studies with larger samples are required to better understand the physiological mechanisms of the observed associations.

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