Elevated Glycosylated Albumin in NIDDM Is a Function of Recent Everyday Environmental Stress

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OBJECTIVE — To evaluate the association of recent daily environmental stress (daily hassles) with glycemia in NIDDM.

RESEARCH DESIGN AND METHODS — Fifty-five NIDDM patients reported the number and intensity of daily hassles occurring during the past week and concurrently underwent glycemic assessment.

RESULTS — Hassles were generally unassociated with demographic variables, illness duration, treatment regimen, and the presence of complications. Multiple regression analysis indicated that hassles (in both frequency and intensity) were positively associated with recent glycemia (glycosylated albumin [GA]), even after statistically controlling for long-term glycemia (glycosylated hemoglobin [HbA_{1c}]). The subtypes of hassles having the most potent relationships with GA were work and family/friend-related stressors.

CONCLUSIONS — The frequency and perceived impact of everyday minor stress have proximal positive associations with glycemia that do not necessarily reflect chronic hyperglycemia. Stress arising from work and family/friend sources may be particularly relevant.

It has been suggested that psychological stress worsens NIDDM course by promoting hyperglycemia via sympathetically mediated gluconeogenesis and glycogenolysis (1,2). Stress hyperglycemia has been experimentally elicited in some (3,4) but not all studies (5–8). Although only one controlled trial has demonstrated improved NIDDM status after behavioral relaxation training (9), trials showing no overall effect suggest that baseline elevation in blood glucose (BG) (10), daily stress (11), and trait anxiety (12) may predict positive treatment response.

Stress hyperglycemia has also been studied by focusing on naturally occurring life stress. Although such studies are uncontrolled and do not allow clear causal inference, they may enhance stressor relevance by considering the idiosyncratic stressors occurring in the life of each particular subject. Thus, findings may be more generalizeable to patients' typical environments. Grant et al. (13) found that "undesirable" major life events were associated with poor NIDDM functioning in 70% of patients; one third had stress-BG correlations exceeding $r = 0.40$. Bradley et al. (14) reported increased glycosuria episodes, medication adjustments, and diabetes clinic visits with increased major life stress. Although Griffith et al. detected no overall differences between stressed and unstressed subjects, high stress combined with low social support was associated with elevated glycosylated hemoglobin (HbA_{1c}) (15).

While most naturalistic studies focus on major stressful events, minor events (also known as "daily hassles") may be even more critical, since in healthy populations they correlate with stress hormone metabolites (16) and are more predictive of health status than are major stress events (17). Goetsch et al. (3) found that five out of six NIDDM patients studied had minor stress–BG correlations and that BG rose on high stress days (18). Jaber et al. (19) used a nine-item inventory to assess stress in 19 NIDDM patients on glipizide; stress correlated 0.70 with fasting BG and 0.84 with HbA_{1c}.

These existing studies are limited by small samples and the lack of standardized well-validated stress measures. This study was designed to test the hypothesis that everyday minor stressors are associated with elevated NIDDM glycemia, using a larger sample and a standardized well-validated stress scale. To rule out the possibility that this relationship is an artifact of poor long-term diabetes control, long-term glycemia was also evaluated.

RESEARCH DESIGN AND METHODS

Subjects

Fifty-five subjects were recruited through the Primary Care and Endocrinology Clinics at a large urban U.S. medical center, using the following inclusion criteria: NIDDM of ≤1 year's duration, stable treatment regimen, and the ability to complete questionnaires independently. Sample characteristics are detailed in Table 1.

Measures

Daily stress. Daily stress was measured with the revised Daily Hassles Scale (DHS), which lists 53 potentially stressful areas of everyday life. Test-retest reliability and validity are well documented (A. Delongis, unpublished observations; 21,22). Subjects rated "how much of a hassle" (on a four-point scale) each item was during the preceding week. The frequency (total number of hassles endorsed), intensity (mean of impact ratings), and eight factor scores (household responsibilities, finances, work, environment, home maintenance, health-related, personal life, and family/friends) were computed. Due to predictor-outcome confounding, the "health" item was omitted from the frequency and intensity scores.

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BG, blood glucose; DHS, Daily Hassles Scale; GA, glycosylated albumin.

Table 1—*Sample characteristics and descriptive data*

	Mean ± SD	Percentage
Personal characteristics		
Age (years)	54.4 ± 14.4	
Sex (female)		58
Ethnicity		
Caucasian		36
African-American		57
Hispanic		6
Asian/Pacific Islander		2
Native American		0
Medical characteristics		
HbA_{1c} (%)	10.6 ± 2.0	
GA (%)	5.4 ± 5.3	
NIDDM regimen		
Diet alone		14
Oral hypoglycemic agent		18
Insulin injection		67
Insulin pump		2
NIDDM duration (years)	16.9 ± 11.5	
Comorbid illnesses		
Hypertension		49
Cardiac condition		24
Hyperlipidemia		22
Complications		
Retinopathy		35
Neuropathy		23
Renal disease		15
Psychological characteristics		
Daily hassles frequency	16.2 ± 11.5	
Daily hassles intensity	0.78 ± 0.40	

Data are means ± SD or %.

Glycemia. Long-term glycemia was assessed with HbA_{1c} (boronate affinity high-performance liquid chromotography method). Recent glycemia was assessed by enzyme immunoassay method with glycosylated albumin (GA), a measure of glycosylated protein distinguished from the HbA family by its shorter half-life. Because it assesses average blood glucose over a brief time period of 7–10 days, it is sensitive to the short-term glycemic level and corresponds to the 1-week time frame assessed by the DHS (23).

Procedure

Subjects provided written informed consent according to Internal Review Board-approved protocol. During a research appointment at the Clinical Research Center, each patient independently completed the DHS immediately before providing morning (~7:30 A.M.) fasting blood samples for GA and HbA_{1c}.

RESULTS — Daily hassles frequency and intensity fell within 1.5 standard deviations of normative values previously reported for adult subjects of similar ages (18). Ranked scores were computed for DHS and GA, since these variables had positively skewed distributions. DHS intensity was positively associated with GA but not with HbA_{1c}, age, illness duration, NIDDM regimen (diet alone versus medication), or the presence of any particular complication (see Table 2). DHS frequency also correlated with GA and NIDDM duration but not with medical or demographic characteristics.

Multiple regression analysis was then used to test the hypothesis that recent glycemia is a function of hassles after accounting for chronic glycemia. GA served as the dependent variable, HbA_{1c} was entered first as a covariate, and the hassles level was entered last. As predicted, DHS intensity had a significant effect on GA (regression coefficient $\beta = 0.31$, $P < 0.05$), while HbA_{1c} did not ($\beta = 0.09$, NS). The same pattern was seen for DHS frequency ($\beta = 0.36$, $P < 0.05$). To examine whether the effect occurred for patients below our relatively high mean HbA_{1c}, we reran the regression for subjects with HbA_{1c} <10.6%, but the DHS effect remained. Further, this effect did not seem to be attributable to differences in medication taking, since DHS scores were unassociated with subjects' ratings of their medication adherence ($r = 0.05$, NS). Subsequent correlational analysis explored which of the eight hassles subtypes correlated with GA; significant associations emerged for hassles related to work ($r = 0.43$, $P < 0.01$) and family/friends ($r = 0.31$, $P < 0.05$); no hassles factors correlated with HbA_{1c}. There were no differences in DHS total or factor scores between Caucasians and ethnic minorities (all t values ≤ |1.92|; all two-tailed P values = NS).

Table 2—*Zero-order correlations*

	Age	NIDDM duration	GA	HbA_{1c}	Hassles frequency	Hassles intensity
Age	1.00	—	—	—	—	—
NIDDM duration	−0.10	1.00	—	—	—	—
Glycosylated albumin	−0.34*	−0.50†	1.00	—	—	—
Glycosylated hemoglobin	−0.13	0.11	−0.09	1.00	—	—
Hassles frequency	0.14	−0.38†	0.33*	−0.19	1.00	—
Hassles intensity	−0.16	−0.18	0.31*	−0.10	0.91†	1.00

*$P < 0.05$; †$P < 0.01$.

CONCLUSIONS — The positive daily hassles–GA association suggests that it may be possible for typical everyday stressors to produce transient elevations in NIDDM glycemia. As predicted, recent daily hassles were uncorrelated with long-term glycemia (HbA_{1c}), and the hassles-GA association persisted even when HbA_{1c} was controlled for statistically. This pattern suggests that the proximal stress–GA association is not simply a byproduct of chronically poor metabolic control. The subtypes of hassles having the most potent relationships with GA were work and family/friend-related stressors.

These results lend further support to earlier studies by using a larger sample and a well-validated stress measure. Nonetheless, correlational data cannot be interpreted as firm evidence of stress-induced hyperglycemia, particularly given the difficulty in experimentally demonstrating this phenomenon. One interpretation of this disparity is that life stress arising from work- and family-related stressors is more personally relevant (and therefore more potent) than standardized mental arithmetic stress. Yet, reasonable alternative explanations also exist. Elevated glucose itself may have direct aversive mood effects (24) or may cause patients to feel helpless about controlling their illness. An unmeasured medical factor (e.g., infection) may affect glycemia, or stress may disrupt the performance of self-care tasks such as meal preparation and BG testing.

Future work ought to attempt to test for a long-term stress–glycemia association by sampling stress throughout the HbA_{1c} time frame, a methodology that has been successfully applied in IDDM (25). Other limitations of this study and areas for future work are the consideration of diabetes-specific everyday stressors (5), depressive disorder (26), social support (15), and the coping responses elicited by everyday stressors.

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