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Randomized Controlled Clinical Trial of Blood Glucose Awareness Training (BGAT III) in Switzerland and Germany

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Although both diabetes and the efficacy of medical management are international issues, psycho-educational interventions might be culturally bound. Blood Glucose Awareness Training (BGAT) is a psycho-educational program for patients with type 1 diabetes mellitus. It is focused on improving recognition and management of extreme blood glucose levels, and is the best documented American psycho-educational program for this purpose. A randomized controlled clinical trial of BGAT's long-term benefits in a non-American setting has been lacking. One hundred and eleven adults with type 1 diabetes mellitus from Switzerland and Germany participated. After a 6 months baseline assessment, subjects were randomly assigned to receive either 2 months of BGAT ($n = 56$) or a physician-guided self-help control intervention ($n = 55$). BGAT improved recognition of low ($p = 0.008$), high ($p = .03$), and overall blood glucose ($p = 0.001$), and reduced frequency of severe hypoglycemia ($p = 0.04$), without compromising metabolic control. BGAT reduced both the external locus of control ($p < 0.02$) and fear of hypoglycemia ($p < 0.02$). BGAT was efficacious in reducing adverse clinical events and achieving clinically desirable goals in a European, as well as American setting.

KEY WORDS: blood glucose awareness training; severe hypoglycemia; psycho-educational program; clinical trial; hypoglycemia fear.

INTRODUCTION

The central goal of type 1 diabetes mellitus management is to normalize blood glucose levels while avoiding extreme blood glucose values (hypoglycemia and hyperglycemia). Although the long-term risks associated with hyperglycemia are generally well recognized by patients and health care professionals, the potential hazards of hypoglycemia require more attention (Muhlhauser *et al.*, 2002). During hypoglycemia, significant negative sequelae can occur, including emotional stress for patients (Gonder-Frederick *et al.*, 1997a) and their significant others (Gonder-Frederick *et al.*, 1997b; Stahl *et al.*, 1998), accidents (Cox *et al.*, 2003), and even death (Sovik and Thordarson, 1999). Symptom recognition and accurate detection of extreme blood glucose values are crucial for management of type 1 diabetes mellitus. Symptoms of hyperglycemia and

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Abbreviations:, BGAT: Blood Glucose Awareness Training, T0: baseline, T1: 1–6 months after intervention, T2: 7–12 months after intervention

hypoglycemia may be minimal, misinterpreted or neglected.

Blood Glucose Awareness Training (BGAT) is a psycho-educational self-management program designed to assist adults with type 1 diabetes mellitus to prevent extreme blood glucose values, and better recognize and treat hyperglycemia and hypoglycemia when they occur. BGAT is typically delivered to outpatients in a group format, over an 8 weeks period. The focus is on teaching patients to identify their individual symptoms suggestive of the extreme blood glucose fluctuations (internal cues) as well as when and how to anticipate blood glucose extremes based on food, exercise, and insulin regimens (external cues).

Participants are instructed to read the appropriate chapter immediately before the class, discuss the personal relevance of the text during the class, and between classes perform homework exercises evaluating the personal relevance of the chapter's content. There have been three editions of BGAT, an initial six chapter version that emphasized internal cues, an eight chapter version focusing on both internal and external cues (BGAT II; Cox *et al.*, 1991, 2001), and an updated version incorporating newer insulins and in which Chapter 8 addresses long-term maintenance (BGAT III; Kinsley *et al.*, 1999). The efficacy of BGAT has been well documented in the USA (Cox *et al.*, 1988, 1991, 2001; Kinsley *et al.*, 1999), with benefits including not only improved blood glucose estimate accuracy, but a dramatic decrease in automobile accidents as well.

However, a European study evaluating BGAT I (Broers *et al.*, 2002) found it to significantly reduce fluctuations in blood glucose but only marginal benefits in improving detection of hypoglycemia and raising questions regarding treatment generalizability. In addition, cultural differences in the applicability of psycho-educational approaches might lead to varying efficacy in a European setting. Therefore, a randomized controlled prospective study of BGAT in European settings was undertaken.

The following hypotheses were tested: (1) BGAT III would lead to improved blood glucose estimation, (2) a reduction in the frequency of extreme blood glucose levels, (3) decrease in the frequency of severe hypoglycemia; and (4) improved psychological functioning in terms of greater internal locus of control and less fear of hypoglycemia. In addition, the effect of BGAT on relevant psychological variables was examined.

SUBJECTS, MATERIALS AND METHODS

Subjects and Research Centers

The research was approved by the Ethics Committee of the Basel University Hospital. Six sites in Switzerland and Germany participated in this prospective multi-center study (see appendix for details). Study information was made available to type 1 diabetes mellitus subjects by conventional mail, oral communications, and posters located in the diabetes specialist's office at each site, regardless of severe hypoglycemia history. However, patients known to the physicians as having recurrent severe hypoglycemia were (often successfully) encouraged to participate. The estimated number of type 1 diabets mellitus subjects being aware of this program is about 400. However, it is impossible to determine the exact number. Subjects who indicated interest were invited to a group information session. Those deciding to participate in the study were individually interviewed, as were their diabetes specialists and/or family physicians (focusing on their diabetes treatment, diabetes complications, and psychiatric comorbidity).

Exclusion criteria were uncontrolled physical (i.e., heart or vascular disease) and mental diseases (i.e., depression, eating disorder, and substance abuse) at the time of claimed interest in the program. Somatic comorbidity was assessed by diabetes specialist or family physicians. Diabetes specialists or family physicians transferred their patients to psychiatrists or the psychosomatic medicine outpatient clinic in case of suspected psychiatric or psychosomatic comorbidity. Comorbidity was considered uncontrolled when newly diagnosed or new treatment had to be established within the last 3 months prior to supposed study entry. Study entrance had to be retarded in six patients because of these criteria. Substance dependency and illicit drug use was assessed by self-report data: any use of cannabis products, benzodiazepines, or barbiturates within the last 2 years, and more than 30 g ethyl alcohol per day. Interestingly, in this sample of middle-aged type 1 diabetes mellitus subjects there was no case qualifying for these criteria.

It was verified that the subjects were on a 'state of the art' intensified insulin regimen, performed three to five injections and at least three blood glucose measurements per day, had a recent adjustment of insulin dose and dosing schedule (if necessary), and routine determination of

glycosylated hemoglobin (HbA1c) every 3 months. All patients provided informed consent and were made aware of their right to discontinue participation in the study at any time.

Study Design

A total of 138 subjects decided to participate in the study. After a 6-month baseline assessment period (T0), subjects were randomly assigned to receive either BGAT or to participate in a physician-guided self-help group (control). Because age and diabetes mellitus duration (Gold *et al.*, 1997) are important confounders favoring the occurence of severe hypoglycemia, subjects were matched to controls within each research center for approximate age and duration of diabetes. At each research center, at least one BGAT group and one control group intervention were offered. The randomization procedure was as follows: within each research center, patients were grouped as pairs of approximately the same age and diabetes duration. Then, a random decision was made as to who of the two patients received BGAT. The other patient received the control group intervention.

Fourteen subjects attended fewer than 50% of the training sessions (eight in the control group and six in the BGAT group) and were not included in the statistical analyses. The two post-intervention measurement periods were at 1–6 months (T1) and 7–12 months (T2) post-intervention. Data was collected at the end of the 6 months period. Thirteen subjects (six controls) who were noncompliant with these follow-up examinations were also excluded from analyses. Baseline characteristics of the drop-out patients and the remaining 111 subjects (80% of all randomized subjects) are reported in Table I, they did not differ between participating subjects and drop-out patients. However, glycosylated hemoglobin of drop-outs was 7.26% (0.99) indicating worse metabolic control in these subjects (Savage non-parametric two-sample test: $p = 0.05$).

Sixty-one percent of the patients had a cohabiting partner. Patients with partners did not differ from patients without partners in hypoglycemic event rate. However, patients with partners had lower glycosylated hemoglobin, especially those patients without severe hypoglycemia in the previous 2 years. The influence of partnership on diabetes-related psychosocial functions will be the focus of another manuscript currently in preparation.

Interventions

The German version of BGAT III (Lübeck Institute for Behavioral Medicine, Fleischhauerstr. 26, 23552 Lübeck, Germany) was delivered by a physician–psychologist team to groups of 5–12 subjects in eight weekly sessions. To assure sufficient quality across study sites, one of the two BGAT group leaders was a trained psychologist from the Basel core study team. Each BGAT session lasted for about 2 h. The introductory session (Chapter 1) is followed by three sessions focusing on the so-called 'internal cues' (physical symptoms; Chapter 2), disruptions in cognitive and motor performance (Chapter 3), and mood changes (Chapter 4). Patients are taught to use these signals to more accurately recognize when their blood glucose is too high or low. The next three chapters focus on how to use 'exogenous cues': previous insulin injections (Chapter 5), food consumption (Chapter 6), and physical exercise (Chapter 7) to better anticipate when blood glucose is likely to rise or fall. Chapter 8 reviews the subject's personal observations from BGAT and discusses ways to maintain BGAT ben-

Table I. Baseline Characteristics

Variable	BGAT ($n = 56$)	Control ($n = 55$)	Drop-outs ($n = 27$)
Sex (female/male)	25/31	21/34	12/15
Age (years)	45 (14.4)	47.9 (13.1)	48.1 (13.4)
Diabetes duration (years)	23.1 (12)	22.7 (12.2)	22.5 (13.9)
Body mass index (kg/m^2)	24.5 (4.5)	23.4 (3.5)	24.2 (4.1)
During last 2 years before study			
Patients with severe hypoglycemia (%)	64	47	50
Patients with hypoglycemic coma (%)	28	25	33
During last 6 months before study			
Motor vehicle accidents (n)	2	2	0
Hospitalization (any cause) (n)	5	6	7
Diabetic ketoacidosis (n)	0	1	1

Note. Severe hypoglycemia (help of others required), Means and SD is reported.

efits. Weekly homework and preparatory readings were required.

The self-help control group was guided by one physician. Five to twelve subjects participated in three monthly sessions. Each control group session lasted for about 2 h. The focus of the sessions was: 'current problems related to diabetes,' 'stress and diabetes,' 'anatomy and physiology,' 'physical activity,' 'diabetes in the workplace,' 'relationship conflicts,' and 'previous experiences'; however, participants determined the specific issues and timing. There was no homework assigned to the control group.

Dependent Variables

All the subjects were instructed to use 2 month diaries developed for this study. Diaries were such that patients could easily insert date and time of measurement, blood glucose estimation, actual blood glucose values, and remarks. Important telephone numbers and mailing addresses (study center, psychologists) were provided on the inside of the cover pages. Patients tested blood glucose at least three times daily. The testing schedule was subject to individual patient—physician communications. However, most of the patients tested blood glucose four times: fasting blood glucose (after awakening), pre-prandial blood glucose values (before supper and lunch), and before bed-time. BGAT did not affect the number of blood glucose measurements. Severe hypoglycemia was defined as any hypoglycemic episode for which the help of others was required (Tattersall, 1999). Severe hypoglycemia was assessed by means of these blood glucose diaries, as well as questionnaires at 6 and 12 months assessments. Diaries and questionnaires gave the same results, with only some exceptions. If necessary, patients, partners, and physicians were interviewed to clarify discrepant reports. It was not possible to routinely verify hypoglycemic events against glucometer results because of logistic difficulties. Sixty-one percent of patients shared their household with a partner. Cohabiting partners were always contacted when severe hypoglycemia was reported as to verify the occurrence of this event. Hand-held computers (Clarke *et al.*, 1995) are known to increase the reliability of blood glucose estimations, but do not guarantee correct report of actual blood glucose values. They were not used in the current study. A period of at least 3 consecutive weeks with complete data pairs of blood glucose estimations and measurements was necessary for each individual patient and assessment point for the subject to be included in analyses. Blood glucose accuracy index (Clarke *et al.*, 1987; Cox *et al.*, 1989), detection of low (< 4 mmol/L) and high (> 10 mmol/L) blood glucose levels, as well as low and high blood glucose risk index (Cox *et al.*, 1994b; Kovatchev *et al.*, 1998) were calculated according to the published standards. Blood glucose thresholds for hypoglycemia symptoms were reported by the subjects based on regular self monitoring blood glucose, they represent subjective estimates.

Standardized questionnaires were used to assess diabetes specific locus of control (Kohlmann *et al.*, 1995), and both diabetes specific (Bradley, 1994; The DCCT Research Group, 1988) and general (Dahlbert, 1992) quality of life measures.

The diabetes-specific locus of control questionnaire was used at T0 and T2, only. It measures four distinct scales: internalization, externalization, unpredictability, and chance control. Internal consistencies range between (Cronbach's alpha) 0.79 and 0.83. Test–retest reliability scores (6 months interval) range between $r = 0.72$ and $r = 0.78$. This questionnaire is available in German, only (Kohlmann *et al.*, 1995).

The Well-Being Questionnaire from Bradley is a validated 22-item instrument containing no somatic items to minimize potential direct effects of poor metabolic control. It was developed specifically for use with diabetic individuals and has been shown to have good reliability and validity (Bradley, 1994). It produces four subscales that assess depression, anxiety, positive well-being, and perceived energy over the previous 7 days. The Well-Being Questionnaire has been applied successfully in the recent research (Paschalides *et al.*, 2004).

The specific Diabetes Quality-of-Life questionnaire was developed for insulin-treated diabetes patients. It measures the scales: satisfaction, impact and diabetes-related worry. All scales were found to have high internal consistencies between 0.66 and 0.92 and excellent test–retest reliability between $r = 0.78$ and $r = 0.92$ (The DCCT Research Group, 1988).

A 19-item mood questionnaire was also employed which is available in German, only. It measures 4 scales (fatigue, hopelessness, negative mood, and positive mood), validation studies revealed internal consistencies ranging between 0.83 and 0.94 (Dahlbert, 1992).

The patients also completed the Hypoglycemia Fear Survey (Irvine *et al.*, 1994) 'worry' and 'behavior' subscales. The Hypoglycemia Fear Survey

worry subscale is based on reactions to severe hypoglycemia episodes (Gold *et al.*, 1997). Thus, the impact of BGAT on fear of hypoglycemia was analyzed in the subsample of patients who had experienced a severe hypoglycemic episode within the 2 years, prior to participation in this study.

Glycosylated hemoglobin (HbA1c; upper limit of normal range: 6.1–6.3%) was determined by an immuno-enzymatic method (DCA, 2000); this data was provided by diabetes specialists or family physicians.

Statistical Analysis

A repeated measures Analysis of Variance (ANOVA) was used to examine the impact of treatment (between subjects factor: BGAT vs. Controls) and time (within subjects factor: Baseline/T0 vs. 1–6 month/T1 vs. 7–12 month/T2 follow-up). The primary statistic of concern was a significant interaction term. Contrasts were constructed *a priori* for comparison of T1 vs. T0 and T2 vs. T0. Including 'severe hypoglycemia in the previous 2 years' as a covariate in the model did not have a significant effect on the results, so to preserve statistical power, the covariate was not included in the final model.

Mean and standard deviation (SD) are reported in tables and text. All the testings were two-tailed. Statistical calculations were performed using SAS (Version 8, WinNT, SAS Institute, Cary, NC, USA).

RESULTS

There was a marginal tendency (chi square statistic, $p = 0.07$) for a greater prevalence of severe hypoglycemia during the 2 years before entry into the study in the BGAT group. The incidence of motor vehicle accidents, hospitalization for any cause, and diabetic ketoacidosis was low in both groups (see Table I). Age, diabetes duration, and body mass index were comparable between groups (see Table I).

The blood glucose estimation and measurement pairs per subject and assessment period (BGAT-T0: 233 ± 195 [$n = 54$], T1: 221 ± 124 [$n = 45$], T2: 203 ± 129 [$n = 46$]; CNT-T0: 233 ± 90 [$n = 50$], T1: 221 ± 127 [$n = 46$], and T2: 203 ± 123 [$n = 47$] (mean $\pm$ SD)) were sufficiently numerous and comparable in time and between groups.

BGAT led to a decrease in severe hypoglycemic episodes and increased recognition of low and high blood glucose levels, so as to improve accuracy index and subjective recognition threshold for hypoglycemia symptoms (see Table II). Extreme blood glucose fluctuations and glycosylated hemoglobin were not influenced by treatment (see Table II). Locus of control became less external, and treated subjects also experienced less unpredictability related to diabetes (see Table III). The behavior-subscale scores of the Hypoglycemia Fear Survey decreased in the BGAT group (indicating less endorsement of behaviors related to hypoglycemia fear), but initial values were higher in this group, so the results might or might not be due to the intervention. There was no impact of BGAT on the Hypoglycemia Fear Survey worry subscale when the entire sample was analyzed (see Table IV). However, when only patients with a history of severe hypoglycemia were analyzed, scores on the worry subscale indicated a reduction in fear for the BGAT group (see Table IV). There was no overall effect of BGAT on either diabetes specific or general quality of life measures.

DISCUSSION

The present study demonstrates BGAT's efficacy in reducing adverse clinical events (severe hypoglycemia), without compromising metabolic control and achieving clinically desirable goals (improved recognition of low and high blood glucose, reduced external locus of control and reduced fear of hypoglycemia) in European settings.

The results of this study are in accordance with previous findings in USA type 1 diabetes mellitus samples. BGAT has been shown to improve the accuracy of blood glucose estimation and detection of hypoglycemia (Cox *et al.*, 1994a, 2001), improve decisions to treat low blood glucose and not to drive while experiencing low blood glucose levels (Cox *et al.*, 2001), reduce frequency of severe hypoglycemia (Cox *et al.*, 1995, 2001), reduce frequency of ketoacidosis (Cox *et al.*, 2001) and motor cycle accidents (Cox *et al.*, 1994a, 2001), reduction in fear of hypoglycemia and increased quality of life (Cox *et al.*, 2001), and improve the counter-regulatory response to hypoglycemia (Kinsley *et al.*, 1999). We now can add that BGAT reduced external locus of control and increased predictability concerning diabetes-specific issues, and that BGAT increased hypoglycemia symptom thresholds.

Hypoglycemia unawareness is a major contributor to the problem of severe hypoglycemia. BGAT has been demonstrated to increase the blood glucose awareness effectively in the USA, but a Dutch report

Table II. Effects of BGAT on Hypoglycemia Rate, Recognition of BG Levels, and Metabolic Control

Variable	T0	T1	T2	Time × Group interaction; *F*, *p*	Contrast T1 vs. T0 group effect; *F*, *p*	Contrast T2 vs. T0 group effect; *F*, *p*
Negative consequences						
Severe hypoglycemia (episodes/6 months)						
BGAT ($n=56$)	1.61 (3.49)	0.13 (0.33)	0.13 (0.33)	$F(2,218)=3.14$	$F(1,109)=1.73$	$F(1,109)=4.04$
Control ($n=55$)	1.76 (3.71)	1.07 (2.85)	1.78 (4.56)	$p=0.04$	$p=0.19$	$p=0.04$
Recognition of BG levels						
Percent detection of low blood glucose levels						
BGAT ($n=33$)	52.7 (21.8)	58.2 (24.8)	65.2 (25.2)	$F(2,132)=4.92$	$F(1,66)=3.79$	$F(1.66)=8.39$
Control ($n=35$)	53.5 (28.0)	45.8 (28.7)	48.0 (25.5)	$P=0.008$	$p=0.05$	$p=0.005$
Percent detection of high blood glucose levels						
BGAT ($n=33$)	45.0 (23.6)	53.1 (25.0)	53.7 (26.2)	$F(2,126)=3.54$	$F(1,63)=5.93$	$F(1,63)=2.62$
Control ($n=32$)	38.8 (24.0)	33.5 (24.8)	38.2 (23.5)	$p=0.03$	$p=0.02$	$p=0.11$
Accuracy Index						
BGAT ($n=37$)	38.8 (17.1)	45.1 (21.6)	47.3 (21.7)	$F(2,144)=7.04$	$F(1,72)=5.21$	$F(1,72)=11.37$
Control ($n=37$)	38.5 (17.5)	35.9 (18.5)	34.6 (19.5)	$p=0.001$	$p=0.02$	$p=0.001$
Subjective hypoglycemia symptom threshold						
BGAT ($n=44$)	3.08 (0.73)	3.38 (0.64)	3.30 (0.72)	$F(2,178)=2.97$	$F(1,89)=5.10$	$F(1,89)=1.45$
Control ($n=47$)	3.25 (0.83)	3.29 (0.75)	3.34 (0.70)	$p=0.05$	$p=0.02$	$p=0.23$
Extreme BG fluctuations						
Low blood glucose index						
BGAT ($n=43$)	2.99 (1.54)	2.48 (1.34)	2.61 (1.32)	$F(2,170)=0.52$	$F(1,85)=0.76$	$F(1,85)=0.67$
Control ($n=44$)	2.62 (1.43)	2.33 (1.44)	2.49 (1.73)	$p=0.60$	$p=0.39$	$p=0.42$
High blood glucose index						
BGAT ($n=43$)	6.53 (3.29)	6.64 (3.37)	6.29 (2.82)	$F(2,170)=0.77$	$F(1,85)=0.00$	$F(1,85)=1.08$
Control ($n=44$)	5.85 (2.92)	5.95 (3.64)	6.17 (3.35)	$p=0.46$	$p=0.99$	$p=0.30$
Glycosylatad hemoglobin (HbA1c)						
BGAT ($n=53$)	6.93 (0.82)	6.93 (1.02)	6.93 (0.96)	$F(2,202)=0.06$	$F(1,101)=0.09$	$F(1.101)=0.03$
Control ($n=50$)	6.91 (0.94)	6.95 (0.98)	6.94 (0.94)	$p=0.94$	$p=0.76$	$p=0.85$

Note. Severe hypoglycemia (help of others required), BGAT: Blood Glucose Awareness Training, Baseline (T0), 1–6 months (T1), and 7–12 months (T2) follow-up, Means and SD is reported.

(Broers *et al.*, 2002) questioned theeffectiveness of BGAT. Those investigators tested BGAT in group vs. individual settings and found the short-term effects of BGAT to be beneficial, but rather modest,

Table III. Effects of BGAT on Locus of Control

Variable	T0	T2	Time × group interaction; *F*, *p*
Locus of control			
Internalization			
BGAT ($n=54$)	38.9 (6.6)	38.6 (7.1)	$F(1,101)=0.00$
Control ($n=49$)	38.4 (6.4)	38.1 (6.6)	$p=0.96$
Externalization			
BGAT ($n=54$)	22.4 (7.8)	20.4 (8.0)	$F(1,101)=5.43$
Control ($n=49$)	19.5 (8.4)	19.8 (8.6)	$p=0.02$
Chance control			
BGAT ($n=54$)	9.2 (4.6)	8.8 (4.4)	$F(1,101)=0.10$
Control ($n=49$)	9.5 (4.9)	9.4 (5.2)	$p=0.75$
Unpredictability			
BGAT ($n=54$)	27.9 (8.2)	24.1 (8.1)	$F(1,101)=14.6$
Control ($n=49$)	26.5 (8.4)	27.2 (8.9)	$p=0.0002$

Note. BGAT: Blood Glucose Awareness Training; the Locus of Control questionnaire was not applied at T1, Baseline (T0) and 7–12 month (T2) follow-up, Means and SD is reported.

suggesting that differences between the American and European samples might affect the reaction to BGAT. However, those investigators did not assess long-term effects and used a briefer version of BGAT (six sessions instead of eight) which might have accounted for the actual difference. Their negative finding may also be explained by a lack of power.

Hypoglycemia is the limiting factor in diabetes insulin therapy (Cryer, 1994). A recent analysis estimated the annual rate of severe hypoglycemic episodes (requiring the help of others) to be 1.5 per patient in a nonselected population of type 1 diabetes mellitus patients, 82% of whom were on intensified insulin therapy (ter Braak *et al.*, 2000). Our sample had twice this incidence of severe hypoglycemia, possibly because our samples are older, have longer diabetes mellitus duration, are receiving intensified insulin treatment, and were selectively encouraged to participate in the study if known to suffer from recurrent severe hypoglycemia.

Surprisingly, some BGAT effects were observed at T1, and others (such as the reduction of severe hy-

Table IV. Effects of BGAT on Fear of Hypoglycemia

Variable	T0	T1	T2	Time × Group Interaction; F, p	Contrast T1 vs. T0 Group effect; F, p	Contrast T2 vs. T0 Group effect; F, p
Hypoglycemia fear survey						
Entire sample						
Worry						
BGAT ($n=53$)	16.5 (12.2)	15.2 (12.1)	13.2 (9.9)	$F(2,198)=1.03$	$F(1,99)=0.01$	$F(1,99)=1.39$
Control ($n=48$)	15.7 (11.7)	14.6 (12.2)	14.7 (12.9)	$p=0.36$	$p=0.93$	$p=0.24$
Behavior						
BGAT ($n=51$)	14.1 (9)	13.7 (8.2)	11.6 (6.9)	$F(2,194)=3.47$	$F(1,97)=0.25$	$F(1,97)=4.85$
Control ($n=48$)	11.3 (6.6)	11.6 (6.4)	12.2 (8.5)	$p=0.03$	$p=0.62$	$p=0.03$
Positive history of severe hypoglycemia within last 2 years						
Worry						
BGAT ($n=33$)	20.6 (12.8)	18.8 (12.5)	15.3 (9.9)	$F(2,106)=4.42$	$F(1,53)=2.13$	$F(1,53)=7.48$
Control ($n=22$)	17.2 (12.1)	19.1 (14.8)	19.3 (12.9)	$p=0.01$	$p=0.15$	$p=0.01$
Behavior						
BGAT ($n=32$)	16.3 (9.1)	15.1 (8.7)	12.6 (7.9)	$F(2,104)=4.1$	$F(1,52)=1.24$	$F(1,52)=6.46$
Control ($n=22$)	12.4 (8.1)	13.5 (7.5)	14 (8.7)	$p=0.02$	$p=0.27$	$p=0.01$

Note. BGAT: Blood Glucose Awareness Training, severe hypoglycemia (help of others required), Baseline (T0), 1–6 month (T1) and 7–12 month (T2) follow-up, Means and SD is reported.

poglycemia) only at T2. Intensified care provided by the physician at study entry, or other unspecific study effects may have been responsible for the low frequency of severe hypoglycemia at T1 in both the groups. The increase of severe hypoglycemia rate in the control group at T2 suggests that this benefit disappeared after another 6 months, when only BGAT effects were of significant duration. This is consistent with the previous research which indicated that 12-months follow-up effects of BGAT were present regardless of whether booster sessions were offered or not (Cox *et al.*, 2001). BGAT improved the percent detection of high blood glucose values and increased subjective hypoglycemia symptom thresholds at T1, only. Statistical significance at T2 may have been missed as a consequence of limited power.

Several limitations of this study have to be considered. It is possible that participants in the BGAT arm of the study received more physician attention (two group leaders) than those in the control group condition (one physician). Furthermore, the treatments were not of equal length and control participants were not asked to complete homework assignments. Additionally, hypoglycemia was not an obligate topic in the control group meetings. The appropriateness of the control group intervention is often subject to discussion in behavioral intervention trials. Ethical considerations do not allow for the implementation of inefficient control treatments. Although blinding of interventions is often advocated, behavioral treatments cannot be delivered in a truly blinded fashion. Crossover studies, where patients serve as their own controls, are frequently complicated by the fact that behavioral treatments, especially cognitive oriented interventions, have long lasting effects without return to baseline. Furthermore, behavioral treatments as well as control interventions may be sensitive to cultural differences. These problems cannot be solved within one trial. Only the homogeneity of different studies from different cultural backgrounds allows for the generalization intended.

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Appendix

The following centers participated in the study: Basel University Hospital (HS, KH, WB and UK), diabetes outpatient center practice, Olten (MS), diabetes clinic, Bad Mergentheim (NH), diabetes

outpatient center practice, Solothurn (Ernst Iff), diabetes outpatient center practice, Aarau (Jürg Lareida), diabetes outpatient center practice, Winterthur (Elisabeth Nützi), diabetes outpatient center practice, Luzern (Frank Ackermann), and Kantonspital Luzern (Christoph Henzen).

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