Rev Med 48:489–509, 1997
5. Marsden PA, Heng HHQ, Scherer SW, Stewart RJ, Hall AV, Shi XM, Tsui LC, Schappert KT: Structure and chromosomal localization of the human constitutive endothelial nitric oxide synthase gene. *J Biol Chem* 268:17478–17488, 1993
6. Hingorani AD, Liang CF, Fatibene J, Parsons A, Hopper RV, Trutwein D, Stephens NG, O'Shaughnessy KM, Brown MJ: A common variant of the endothelial nitric oxide synthase gene is a risk factor for coronary atherosclerosis in the East Anglian Region of the UK (Abstract). *Circulation* 96 (Suppl. 8):545, 1997

Influence of a Physical Training Program on Psychological Well-Being in Elderly Type 2 Diabetes Patients

Psychological well-being, physical training, and type 2 diabetes

Physical activity is positively associated with mental health and psychological well-being, but so far only a few studies have investigated the association between physical activity and psychological factors in patients with diabetes (1,2). In a cross-sectional study in this group of patients, of whom the majority had type 2 diabetes, the level of physical activity turned out to be the only significant self-management behavior to predict quality of life (2). We were interested in the effects of a physical training program on psychological well-being in these patients. The present study was part of a prospective randomized trial to evaluate the effects of physical training on glycemic control and lipid profile in elderly obese type 2 diabetes patients (3). We hypothesized first that aerobic physical training results in an improved psychological well-being and second, that an improved psychological well-being is mediated by changes in the maximal aerobic capacity (Vo_{2max}).

There were 92 patients with type 2 diabetes who applied for the study. Of these, 58 enrolled and were randomized to either a physical training group (TG) (n = 30; aged 64.2 ± 5.4 years [mean ± SD]) or a control group (CG) (n = 28; aged 61.8 ± 5.4 years). There were 51 patients who completed the study. The training program consisted of an intensive supervised 6-week physical training period in which the patients exercised three times a week for 1 h, aiming at 60–80% of their Vo_{2max}. This period was followed by a 6-week guided home training period. The control group followed a diabetes education program during that time. In the 14-week follow-up phase, patients in the training group were advised to continue their home training, but without supervision. Psychological well-being was assessed by means of the 22-item self-administrated well-being questionnaire of Bradley and Lewis (4), which was completed at baseline, after 6 weeks of training, and at the end of the study. Items referring to physical symptoms possibly related to diabetes were excluded to obtain a pure estimate of the psychological domain of well-being. The scores of the questionnaire were determined by four subscales: depression, anxiety, energy, and positive well-being. A repeated measures analysis of variance with polynomial contrasts was used to determine differences in well-being. To test for Vo_{2max} as a mediator variable, regression analyses were performed according to Baron and Kenny (5).

At baseline, no differences between TG and CG were found with respect to age, BMI, duration of disease, sex, physical activity status, smoking habits, HbA_{1c}, Vo_{2max}, the total psychological well-being score, or the four subscales. After 6 weeks of training, a significant improvement was found in TG for total psychological well-being (baseline: 49.2 ± 11.2 [TG], 45.3 ± 14.4 [CG]; after 6 weeks: 54.8 ± 7.6 [TG], 46.9 ± 14.2 [CG]; F = 5.46, P = 0.023), anxiety (baseline: 5.0 ± 4.1 [TG], 5.3 ± 4.0 [CG]; after 6 weeks: 2.8 ± 3.2 [TG], 5.3 ± 4.3 [CG]; F = 7.80, P = 0.007), positive well-being (baseline: 13.9 ± 4.3 [TG], 11.5 ± 5.1 [CG]; after 6 weeks: 14.4 ± 3.1 [TG], 12.2 ± 4.7 [CG]; F = 6.37, P = 0.014), and energy (baseline: 8.0 ± 2.4 [TG], 7.9 ± 3.5 [CG]; after 6 weeks: 9.4 ± 2.1 [TG], 8.0 ± 3.0 [CG]; F = 4.88, P = 0.031). For depression, no significant difference was found. After 6 weeks of training, a significant difference in Vo_{2max} levels emerged between TG and CG ($P < 0.01$) and remained significant until the end of the study, although the scores of TG decreased (TG: 21.0 [prestudy], 22.0 [after 6 weeks], and 21.0 ml · kg^{-1} · min^{-1} [after 26 weeks]; CG: 20.8 [prestudy], 19.6 [after 6 weeks], and 18.2 ml · kg^{-1} · min^{-1} [after 26 weeks]). The Vo_{2max} difference score was used in the analysis as a mediator variable for total psychological well-being, but no mediation could be observed.

It is important to note that after the supervised period of 6 weeks, well-being scores returned to baseline levels. It is possible that changes in compliance with the training program caused the declining scores of Vo_{2max} and well-being at the follow-up measurements. Several factors can influence compliance with training programs, e.g., group participation, spouse support, and periodic testing. It is imaginable that the decreased support and attention for the training group during the unsupervised period caused the declining well-being scores. Another explanation may be that physical training benefits the physiological response to stress (6). The initial improvements in aerobic capacity coupled with the psychological well-being scores and the subsequent return to baseline values of both parameters seems to support this view. However, no statistical proof of direct influence of Vo_{2max} on improvement of quality of life could be obtained. Finally, a cognitive explanation for the stress-reducing effects of physical training can be given (7). Training may affect feelings of self-esteem, as a result of the mastering and the increased performance of challenging physical activities, and subsequently improve well-being. When the initially positive excitement and actual performance decline, the positive psychological effects may subside as well. Based on the results of the present study, it seems that feelings of well-being, presumably related to self-efficacy or self-esteem, are only positively affected by a training program when the participant's actual performance of the training activities is continued.

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References
1. Kaplan RM, Hartwell SL, Wilson DK, Wallace JP: Effects of diet and exercise interventions on control and quality of life in non-insulin-dependent diabetes mellitus. *J Gen Int Med* 2:220–227, 1987
2. Glasgow RE, Ruggiero L, Eakin EG, Dryfoos J, Chobanian L: Quality of life and associated characteristics in a large national sample of adults with diabetes. *Diabetes Care* 20:562–567, 1997
3. Ligtenberg PC, Hoekstra JBL, Zonderland ML, Bol E, Erkelens DW: Effects of physical training on metabolic control in elderly type 2 diabetes mellitus patients. *Clin Sci* 93:127–135, 1997
4. Bradley C, Lewis KS: Measures of psychological well-being and treatment satisfaction developed from the response of people with tablet-treated diabetes. *Diabet Med* 7:445–451, 1990
5. Baron RM, Kenny DA: The moderator-mediator variable distinction in social psychological research: conceptual, strategic, and statistical considerations. *J Pers Soc Psych* 51:1173–1182, 1986
6. Blumenthal JA, Emery CF, Walsh MA, Cox DR, Kuhn CM, Williams RB, Williams RS: Exercise training in healthy type A middle-aged men: effects on behavioral and cardiovascular responses. *Psychosom Med* 50:418–433, 1988
7. Long BC: A cognitive perspective on the stress-reducing effects of physical exercise. In *Exercise Psychology: The Influence of Physical Exercise on Psychological Processes*. Seraganian P, Ed. New York, Wiley, 1993

Fatal Asymptomatic Hypoglycemia in an Elderly Insulin-Dependent Diabetic Patient Taking an Oral Beta-Blocking Medication

The largest study of the risk of serious insulin- or oral hypoglycemic–related hypoglycemia involving all classes of antihypertensives recently reported that the lowest rate of hypoglycemia over a 4-year study period in 13,559 elderly Medicaid recipients was with beta blockers. The highest rate of serious hypoglycemia was found to be with ACE inhibitors used with antidiabetic agents (1). A 1966–1998 Medline search using the terms beta blockers, insulin, and hypoglycemia produced one case report of topical timolol-associated hypoglycemic attacks in a 65-year-old insulin-dependent diabetic patient (2).

J.P. was a 68-year-old, 5-foot 4-inch, 192-lb, African-American, insulin-dependent diabetic patient who also had high blood pressure, presumed type 1 diabetes, and angina pectoris. Her diet order was 1,600 kcal (American Diabetes Association [ADA]), but her family insisted on bringing in extra food despite numerous warnings about this practice. She had gained 26 lb in the 6 months since her admission to the nursing facility. Her medications were as follows: NPH insulin 42 U subcutaneously every morning at 7:00 A.M., sublingual nitroglycerin 0.4 mg as needed (not used), and propranolol 20 mg q.i.d.. Her fasting blood sugar (FBS) had ranged between 5.7 and 6.8 mmol/l (102–122 mg/dl) weekly for the past month. Her insulin dose had been increased from 20 U on admission to 42 U over the 6-month period in response to monthly FBS readings >8.9 mmol/l (160 mg/dl). When the family went on vacation and the extra food supply was unavailable, on the 3rd day of reduced caloric intake, the patient did not care for the food of the day and was found at 4:00 P.M. semicomatose, with blood pressure (BP) = 158/88, P = 76, R = 26. Her prior weekly vital signs had ranged from BPs of 110–126/60–72 mmHg, pulses of 56–64 beats/min, and respiration rates of 12–20 breaths/min. She died by 5:00 P.M., with a fingerstick blood sugar of <1.4 mmol/l (25 mg/dl). The patient's nursing aides and roommate denied that she had any of the classic symptoms of hypoglycemia (tachycardia, sweating, excitation, nervousness, or tremors) over the prior week or on the day of her death. The nurses' daily notes for the week before death had no mention of any of these symptoms.

A 1980 study of the safety of beta-blocker usage in insulin-treated diabetic patients found, using the surrogate hypoglycemic measure of unconsciousness, that 50 insulin-treated diabetic patients using beta blockers had the same frequency of episodes (5 vs. 10) as 100 insulin-using diabetic patients matched for age, sex, and duration of diabetes who did not use beta blockers over an 8-month period (3). The latest study previously mentioned found that cardioselective beta blockers had the lowest frequency of serious hypoglycemia (<2.8 mmol/l [50 mg/dl]) in older individuals using insulin or sulfonylureas when compared with the nonselective beta blockers, thiazide diuretics, calcium channel blockers, or ACE inhibitors (1). Intensive treatment of type 1 and type 2 diabetes appears to lower the rates of renal impairment, cardiac and overall morbidity, and mortality (4–6). Insulin usage per se does, however, produce higher rates of hypoglycemia and weight gain when compared with oral hypoglycemic agents in an outpatient setting over 6 years (6) and in the nursing home over a 3-year period (7). Intensive insulin therapy for type 1 diabetes also has been found both to increase blood pressure and to adversely affect lipid profiles proportional to weight gain (8).

This patient appeared to have multiple factors that led to her weight gain: insulin use and excessive outside dietary intake. Her complete diabetes history was not obtainable. The family did state that she had tried the "sugar pill," but that she would not take the pill nor adhere to her diet. Her attending physician on admission to the nursing facility was from a different provider than her community-based physician. The nursing facility physician's therapeutic goal was tight control of blood sugar, which he defined as <6.9 mmol/l (125 mg/dl). Beta-blocker therapy for both high blood pressure and angina pectoris was preferred, because of her history of angina pectoris, for presumed secondary prevention of myocardial infarction, since the patient had complained of several episodes of severe chest pain. No electrocardiographic readings were available on this patient.

The extent to which the nonselective beta blocker propranolol masked the hypoglycemic symptoms that may have been more likely with her tight blood sugar control (i.e., <6.9 mmol/l [125 mg/dl]) is suggested by the negative findings on questioning of health care personnel involved in the care of the patient as well as by the clinical record. The patient and her roommate were both well oriented to time, place, and person and did not have clinical evidence of dementia. The roommate was very concerned with the patient's overall care and was known to have summoned help for her roommate if she suspected any problem. The patient was not known to take naps during the daytime hours. It was this roommate who noticed the patient's unusual drowsiness and sedation and reported this to the charge nurse at 4:00 P.M. on the day of death.