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The Effectiveness of an Obstructive Sleep Apnea Screening and Treatment Program in Patients With Type 2 Diabetes

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Abstract

Aims—As recommended by current guidelines, we tested the acceptability and impact of screening patients with type 2 diabetes for obstructive sleep apnea (OSA).

Methods—In a large urban primary care practice, we instituted a telephone-based OSA screening program using a validated tool (STOP-BANG) in patients with type 2 diabetes. Patients identified as high risk were referred for diagnostic sleep testing, and those diagnosed with OSA were offered positive airway pressure (PAP) therapy. We evaluated the impact of PAP on sleep-related symptoms, glycemic control, and hospitalization rates.

Results—We identified 738 of 818 (90.1%) patients with type 2 diabetes as high risk for OSA. Only 29.2% (n=213) of high risk patients were willing to undergo diagnostic sleep testing. The prevalence of OSA was 90.6% in this group, but only 66.0% of those with OSA initiated PAP. Patients with higher burden of sleep symptoms were more likely to pursue testing and initiate therapy. PAP use was associated with reduced sleep-related symptoms (mean Epworth sleepiness scale score declined from 8.8 to 7.3, $p<0.001$), but did not impact hemoglobin A1c levels at one year (7.7 to 7.9%, $p=0.12$). Changes in glycemic control and hospitalization rates did not differ from comparator groups.

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Conclusions—Despite a high prevalence of OSA, willingness to pursue diagnostic testing and treatment was low in an unselected type 2 diabetes population. Furthermore, glycemic control did not improve. Future screening programs should focus on patients with substantial sleep related symptoms as this group is most likely to derive benefit from treatment.

Keywords

Sleep Apnea; Diabetes; Screening

1. Introduction

Obstructive sleep apnea (OSA) is a highly prevalent condition that is associated with excessive daytime sleepiness, reduced quality of life, hypertension, and increased cardiovascular risk.¹ Patients with type 2 diabetes are at particularly high risk for OSA. The Sleep Heart Health Study, a community-based cohort study, observed a 58% prevalence of OSA among participants with type 2 diabetes. Similarly, in a subset of overweight and obese diabetics participating in the LookAHEAD trial, the prevalence of OSA was over 86%.^{2, 3} However, a study using clinical records to confirm OSA diagnosis reported only 18% of type 2 diabetes patients attending primary care clinics had a documented diagnosis of OSA. This suggests that despite the high rates of OSA among patients with type 2 diabetes, OSA is likely substantially under-diagnosed in this population.⁴ Therefore, an OSA screening program based in primary care may have the potential to identify a large proportion of patients with type 2 diabetes suffering from undiagnosed OSA.

OSA increases risk for incident type 2 diabetes independent of obesity,^{5, 6} and a causal role for OSA in the development of diabetes and disease severity is supported by basic research.^{7–9} Uncontrolled studies have suggested improved glycemic control with positive airway pressure (PAP) therapy.^{10–12, 13} However, randomized controlled trials have had mixed results, with clinically important improvements in hemoglobin A1c demonstrated in some, but not all, studies.^{14–16} Furthermore, findings from these studies have limited generalizability to typical type 2 diabetes populations given the strict inclusion criteria of most trials that excluded older patients and those with comorbidities.

A recent retrospective cohort study analyzing clinical data from a general diabetes population reported a large difference in hemoglobin A1c levels between OSA patients who accepted and refused PAP.¹³ However, this effect was due to significant worsening of glycemic control in those refusing PAP as opposed to improvements in those accepting PAP. The authors concluded there was a need for prospective studies evaluating the impact of PAP therapy in general type 2 diabetes populations with OSA.

In light of the significant burden of OSA among patients with type 2 diabetes, the American Diabetes Association, the International Diabetes Taskforce on Epidemiology and Prevention, and the American Academy of Sleep Medicine (AASM) have published clinical guidelines recommending patients with type 2 diabetes undergo routine screening for OSA.^{17–20} These recommendations are based on expert opinion, without data that OSA screening improves diabetes-related outcomes in clinical settings. Furthermore, the recommended methods for screening vary, ranging from inquiring about OSA symptoms^{17, 19, 20} to routine referral of

all patients with type 2 diabetes to a sleep specialist.¹⁸ In this context, we evaluated the feasibility and effectiveness of an OSA screening and treatment program for patients with type 2 diabetes.

2. Methods

2.1 Screening Program

From 2013 to December 2014, we established a clinical pathway to screen all patients with type 2 diabetes for OSA in Healthcare Associates (HCA), a large, hospital-based primary care clinic at Beth Israel Deaconess Medical Center (BIDMC), Boston, MA. HCA includes 65 attending physicians, 99 resident physicians, and 6 nurse practitioners who care for over 42,000 patients. The BIDMC Institutional Review Board approved evaluation of this clinical program with waiver of informed consent.

All HCA patients with type 2 diabetes not receiving OSA treatment were identified using the electronic medical record (EMR). Each primary care provider was given the option to exclude patients from OSA screening due to low likelihood of benefit (e.g., active malignancy). Patients received up to three telephone calls for screening with the STOP-BANG questionnaire by a program coordinator. The STOP-BANG questionnaire consists of 8 yes or no questions that assess OSA risk based on demographic factors, co-morbidities, and symptoms.^{21, 22} Patients at high-risk for OSA (STOP-BANG score $\geq 3/8$) with at least one OSA symptom (e.g. disruptive snoring, daytime sleepiness) were advised to undergo sleep testing. Choice of testing type (laboratory vs. home) was determined in accordance with usual clinical practice, incorporating patient appropriateness for home testing, patient preference and insurance coverage. At the time of this study, home sleep testing was the preferred method of diagnostic testing for most insurance providers in Massachusetts unless a contraindication (e.g. congestive heart failure) was present. Program staff made up to three additional telephone calls to coordinate testing. Staff also assisted with coordination of language interpretation and insurance pre-certification.

All studies were scored using 2007 AASM scoring criteria requiring a 4% drop in oxyhemoglobin saturation for hypopneas.²³ Patients with an apnea hypopnea index (AHI) ≥ 5 events/hr were referred to a board-certified sleep specialist for evaluation. Therapeutic decisions were made with the patient, in accordance with AASM guidelines. All PAP machines (ResMed S9) transmitted daily adherence data to a secure online portal. Staff monitored PAP adherence weekly. Staff trained in motivational interviewing techniques called patients with usage less than 4 hours/night to troubleshoot problems. Patients with ongoing difficulty were scheduled for an additional sleep physician visit. Patients initiating PAP otherwise followed up 6 weeks after PAP initiation.

2.2 Comparator Groups

Patients diagnosed with OSA and prescribed PAP were contrasted with two groups: 1) patients at high-risk for OSA by STOP-BANG who declined sleep testing and 2) patients diagnosed with OSA who declined PAP. The index date for patients who initiated PAP was

the start date for PAP therapy (median of 98 days after screening). The index date for the comparator groups was 98 days following screening.

2.3 Outcome Measures

Data regarding glycemic control and hospitalizations were obtained from the EMR as part of clinical care. Among PAP users, sleep-related symptoms were assessed at each sleep clinic visit. Sleepiness was assessed using the Epworth sleepiness scale (ESS).²⁴ Sleep disturbance and sleep-related daytime impairment were assessed using the 8-item short forms of the NIH Patient-Reported Outcomes Measurement Information System (PROMIS) Sleep Disturbance (PROM-SDA) and Sleep Related Impairment (PROM-SRI) scales, respectively.^{25, 26}

2.4 Covariates and Additional Factors of Interest

Adherence to PAP was defined as use of at least 4 hrs/night over the first 90 days. The Charlson comorbidity index was calculated using ICD-9 billing codes from the 1-year prior to index date.²⁷ Body mass index (BMI) prior to screening was obtained from the EMR. Medication lists were reconciled in the EMR at each clinical visit. Using these data, diabetes medications and their dosages were identified for each patient at the index date and at 1 year. A board certified internist blinded to group status reviewed all changes in agent or dose and classified them as an escalation, de-escalation, or equivalent change.

2.5 Statistical Analysis

Within-patient differences in continuous outcomes were assessed over 90 days and 1 year from the index date using paired t-tests and differences in categorical outcomes were assessed using McNemar's test. Differences between patients who initiated PAP and each comparator group were evaluated separately with unpaired t-tests for continuous and Fisher's exact tests for categorical outcomes. Subsequently, multivariable linear regression was used to assess the impact of PAP therapy on HbA1c at 90 days and 1 year adjusting for baseline value, age, sex, BMI, and baseline HbA1c level. Sensitivity analyses were performed restricting to patients without medication changes. Log-rank tests were used to compare incident hospitalization rates between PAP users and each comparator group. Further analyses used Cox proportional hazards models adjusting for age, sex, BMI, Charlson index and baseline HbA1c level. Secondary analyses limited evaluation to those who used PAP at least 4 hrs/night. All analyses were conducted using SAS 9.4 (Cary, NC).

3. Results

A detailed pathway of patient flow is outlined (Figure 1). 818 patients with type 2 diabetes were contacted and screened. Of these, 738 (90.2%) were high-risk for OSA based on STOP-BANG. However, only 213 (28.9%) of high-risk patients underwent sleep testing. Of patients tested, 193 (90.6%) met criteria for OSA. Of these, 128 (66.3%) patients initiated PAP therapy while 65 patients (33.7%) declined PAP.

On average, patients were late middle age (mean age 63.5 ± 11.6 years), obese (mean BMI 32.5 ± 6.6 kg/m²), and two thirds had neuropathy, nephropathy, or retinopathy related to their diabetes. Mean HbA1c at baseline was 7.7% and was similar across groups. On

telephone screening, those accepting PAP were more likely than those who declined sleep testing to endorse sleep symptoms including feeling tired or sleepy during the day (88.1% vs. 45.6%, $p<0.001$), loud snoring (81.1% vs. 51.3%, $p<0.001$), and observed apneas (24.6% vs. 6.7%, $p<0.001$). Among patients who were diagnosed with OSA, patients accepting PAP had more severe OSA (AHI 25.0 vs. 14.0 events/hr, $p<0.001$), and had greater severity of sleep symptoms by ESS and PROMIS questionnaires (Table 1).

Among patients initiating PAP, average adherence over 90 days was 3.5 (SD 2.5) hours per night. Sleep symptoms improved over 90 days of treatment (Table 2). ESS declined 1.5 points ($p<0.001$), PROM-SRI t-score declined 3.7 points ($p<0.001$) and PROM-SDA t-score declined 4.1 points ($p<0.001$). The proportion of individuals with excessive daytime sleepiness (ESS > 10), fell from 34.6 to 20.2% ($p=0.004$).

Among those who initiated PAP, mean HbA1c rose slightly from 7.7% at baseline to 7.9% at 90 days ($p=0.04$) and 7.9% at one year ($p=0.12$ compared to baseline). These changes did not differ from temporal changes in either of the comparator groups. Our results did not differ in adjusted analyses, or when restricting the PAP group to those adherent to treatment (4 hours/night on average). We also observed no differences in diabetes medication changes between those initiating PAP and comparator groups (Table 3).

The rate of hospitalization in patients initiating PAP therapy was 8.7 per 10,000 person-days, which did not differ significantly from the rates in those who declined PAP (5.1 per 10,000 person-days) or declined sleep study (7.2 per 10,000 person-days). Results did not differ in adjusted analyses.

4. Discussion

In a primary care based sample of patients with type 2 diabetes, over 90% of patients screened were high-risk for OSA, though fewer than one-third of high-risk patients with diabetes agreed to undergo testing. Among those tested, over 90% had OSA but only two-thirds of patients with OSA initiated PAP. Treatment with PAP resulted in improvements in sleep-related symptoms; however, we did not observe improvements in glycemic control or hospitalization rate.

We found a large proportion of type 2 diabetes patients without a clinical diagnosis of OSA were at high risk for this disorder, and among those who agreed to testing, the prevalence of OSA was high. These findings support prior data that OSA is highly prevalent in type 2 diabetes but underdiagnosed.^{3,4} Our results also demonstrate the difficulty of widespread OSA screening, which may underlie this discrepancy. Only 29% of the 738 patients high-risk for OSA completed diagnostic testing. This occurred despite multiple reminder phone calls and dedicated assistance with the logistics of obtaining insurance pre-certification and scheduling sleep studies. The low conversion rate for sleep testing likely reflects referral of patients with few symptoms, and barriers associated with obtaining sleep studies, out-of-pocket payments, wait times, and barriers for overnight visits such as transportation and childcare. A low perception of benefit from OSA diagnosis and treatment, and lack of acceptability of current treatments likely also contributed. A relatively low level of

acceptance of diagnostic sleep testing also has been observed in studies screening for OSA among patients enrolled in cardiac and pulmonary rehabilitation programs, with 38% and 55% of patients returning for testing.^{28, 29} Some parallels can be drawn to universal diabetic retinopathy screening which only occurs in 49 to 56% of patients, with rates lower among those with lower income and racial and ethnic minorities as well as patients who poorly understood the rationale for screening.^{30, 31} Further research to identify and overcome barriers to OSA screening will be necessary to implement more widespread testing.

The greatest benefit of PAP in our study was in sleep-related symptoms. Consistent with prior research,^{15, 16, 32} we observed a significant decline in sleepiness with PAP use. There is a dose response relationship of sleep symptom improvement with PAP adherence,³³ and substantial improvements in symptoms occur with usage of just 2 hrs/night.³⁴ Therefore it is not surprising that sleepiness improved despite our mean usage of 3.5 hrs/night. Although the mean reduction in ESS (1.5 points) does not meet criteria for a minimum clinically important difference,³⁵ we did find clinically important improvements (defined by a 2-point reduction in t-score) in sleep disturbance and sleep-related impairment, as assessed by the PROM-SDI (3.7 points) and PROM-SDA (4.1 points).³⁶ In addition, the proportion of patients with excessive daytime sleepiness (ESS>10) fell by 14% corresponding to a number needed to treat of 7, which also suggests a clinical benefit of PAP therapy in this population. Given the beneficial impact of PAP on sleep-related symptoms and the finding that those with greater burden of sleep symptoms were the most willing to undergo OSA testing and treatment, any OSA screening program in a type 2 diabetes population should focus on those patients with quality of life deficits from poor sleep. Even with such a focus, many patients would benefit, as between 45-70% of patients with type 2 diabetes experience poor quality sleep,^{37, 38} and 24-65% report symptoms of fatigue.³⁹ Further research to identify an optimal screening instrument for OSA is needed, but our data indicate that such an instrument should be focused on severity of symptoms both to maximize treatment benefit as well as to select the group most willing to pursue evaluation and treatment. The STOP-BANG, which focuses on assessing OSA risk rather than severity of symptoms, appears poorly suited for such a role.

Our findings also demonstrate a lack of improvement in glycemic control with PAP therapy. This finding is consistent with the majority of data from randomized controlled trials.^{15, 16} The failure of CPAP to improve glycemic control may be due to several reasons. One possibility is that the level of PAP adherence obtained was insufficient to derive glycemic benefit. A small highly controlled single-arm trial suggested 8 hours of nightly PAP use over 2 weeks can improve fasting glucose levels in patients with type 2 diabetes,¹¹ and a recent observational study in patients without diabetes found a beneficial glycemic effect only in those with PAP usage 8 hrs/night on 90% of nights,⁴⁰ a level of use attained in only 6% of patients. Data from generalizable clinical settings suggest 46-83% of OSA patients use PAP at an average of <4 hrs/night,⁴¹ which is consistent with our findings. Another possibility for our findings is that OSA therapy may be ineffective for improving glycemic control among those with long standing diabetes.¹⁵ Instead, benefit may lie in the prevention of diabetes among at-risk individuals.^{40, 42}

Of note, a retrospective cohort study of type 2 diabetes patients recently diagnosed with OSA reported a large difference in hemoglobin A1c trajectories in those who accepted versus declined PAP therapy. However, this difference was due to a worsening of mean hemoglobin A1c levels (from 7.9% to 13.1% over 1 year) greater than would be expected in the control group suggesting the selection process used to identify those refusing PAP may have preferentially identified patients refusing all treatments including those for their diabetes. Our findings using a prospective study design and broad inclusion criteria provide a clearer assessment of the impact of screening and treating OSA in type 2 diabetes populations encountered in clinical practice.

This study has several limitations. First, the STOP-BANG instrument has not been validated specifically in a type 2 diabetes population. The high proportion of individuals found to have OSA among those screening positive provides some reassurance of the instrument's sensitivity, but we are unable to assess specificity. Another potential limitation is that measures of HbA1c and hospitalizations were collected from the medical record. While minimizing patient burden, the lack of standardization in measurement procedures would tend to reduce power to detect a real effect. However, our use of "real world" assessments provides a more generalizable perspective of the effectiveness of PAP therapy as would be appreciated at a health system level. Screening may also have been more effective if performed in person by the primary care provider as opposed over the phone by staff. However, such provider-driven screening would increase the burden on primary care providers, limiting feasibility.

Despite these limitations, this study addresses an area of important uncertainty. A recent review by the United States Preventive Services Task Force found insufficient evidence to justify routine screening for OSA in all adults.⁴³ The review noted uncertainty regarding the benefit to screening for patients without symptoms or with unrecognized symptoms of OSA. Our results provide direct evidence towards filling this gap in a group at high-risk for OSA. Similarly, investigations that have demonstrated glycemic benefits with OSA treatment in type 2 diabetes have carefully selected for patients most likely to benefit and used aggressive strategies to increase adherence with PAP therapy—limiting generalizability.^{11, 14} By screening all type 2 diabetes patients in a typical academic general medicine practice and using feasible adherence strategies, our work provides the first prospective evidence on the effectiveness of an OSA screening and treatment program as part of usual practice. Such effectiveness studies are particularly necessary with complicated interventions like PAP.⁴⁴

Overall, despite most patients being at high risk for OSA, most patients did not proceed to formal OSA testing and treatment, with treatment benefits limited to improvement in sleep-related symptoms. Therefore, our findings argue against routine screening for OSA in all patients with type 2 diabetes. Our findings indicate that patients with type 2 diabetes who had sleep-related symptoms were the most willing to undergo OSA screening and treatment, and their symptoms were likely to benefit from treatment. Therefore, we believe that future research should focus prioritize developing a brief and easily administered symptom-focused OSA screening tool and then evaluating the impact of deploying such a tool in primary care.

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Highlights/Clinical Significance

- The benefit of screening for obstructive sleep apnea (OSA) is unclear.
- Over 90% of patients with type 2 diabetes were high-risk for OSA.
- Only 17% of high-risk patients initiated OSA treatment.
- OSA treatment improved sleep symptoms, but not glycemic control or blood pressure.
- In the absence of symptoms, there is low value for OSA screening in type 2 diabetes.

Figure 1.

Patient flow through the OSA screening program.

High-risk for obstructive sleep apnea was defined as a STOP-BANG score of greater than or equal to 3. Obstructive sleep apnea was defined as an apnea hypopnea index greater than or equal to 5 events per hour. The three groups compared are noted by **bold text** and asterisk (*). PAP-positive airway pressure. OSA-obstructive sleep apnea.

Table 1

Baseline characteristics of those initiating PAP therapy and two comparator groups.

	Initiated PAP n = 128	Declined PAP n=65	Declined Sleep Study n=525
	mean (SD)/n (%)	mean (SD)/n (%)	mean (SD)/n (%)
Demographics			
Age, yrs	61.6 (11.8)	61.0 (12.3)	64.3 (11.4)*
Female, n (%)	61 (47.7)	42 (64.6)	281 (53.5)
Race/Ethnicity, n (%)			
Non-Hispanic Black	54 (42.2)	26 (40.0)	240 (45.7)
Non-Hispanic White	51 (39.8)	21 (32.3)	191 (36.4)
Hispanic	11 (8.6)	6 (9.2)	41 (7.8)
Other	12 (9.4)		53 (10.1)
Comorbidities and Disease Severity			
BMI (kg/m ²)	33.9 (7.1)	33.4 (7.3)	32.0 (6.4)**
Overall Charlson Score (/15)	3.5 (2.3)	2.9 (2.1)*	3.2 (2.3)
Complication of Diabetes (%)	87 (68.0)	42 (64.6)	345 (65.7)
Renal disease (%)	31 (24.2)	10 (15.4)	110 (21.0)
Myocardial infarction (%)	17 (13.3)	1 (1.5)	39 (7.4)
Congestive heart failure (%)	23 (18.0)	5 (7.7)	58 (11.0)
Cerebrovascular disease (%)	17 (13.3)	3 (4.6)	46 (8.8)
HbA1c (NGSP, %)	7.7 (1.5)	7.4 (1.8)	7.7 (1.8)
HbA1c (IFCC, mmol/mol)	61 (16.4)	57 (19.7)	61 (19.7)
Medication use for Diabetes (%)	84 (66.7)	38 (58.5)	319 (60.8)
Insulin use (%)	36 (28.6)	10 (15.4)	90 (17.1)
Medication use for HTN (%)	98 (77.8)	50 (76.9)	368 (70.1)
Self Reported Symptoms			
Loud Snoring (%)	103 (81.1)	49 (76.6)	269 (51.3)**
Tired, Fatigued or Sleepy (%)	111 (88.1)	51 (79.7)	239 (45.6)**
Observed apneas (%)	31 (24.6)	12 (18.8)	35 (6.7)**
Sleep Measures			
ESS (score/24)	8.8 (5.2)	6.1 (4.8)**	—
PROM-SDA (t-score)	54.5 (6.5)	51.6 (6.3)*	—
PROM-SRI (t-score)	54.1 (9.7)	46.9 (11.4)**	—
AHI (events/hour)	25.0 (23.5)	14.0 (14.7)**	—
AHI 15/hour (%)	63 (49.2)	19 (29.2)**	—
AHI ≥30/hour	37 (28.9)	8 (12.3)**	—

* - p < 0.05,

** -p<0.01 for differences from the initiated PAP group.

BMI-body mass index; HbA1c-glycated hemoglobin; HTN-hypertension; ESS-Epworth sleepiness scale; PROM-SDA-Patient Reported Outcome Measure Information System (PROMIS) Sleep Disturbance instrument (t-score); PROM-SRI-Patient Reported Outcome Measure Information System (PROMIS) Sleep Related Impairment instrument (t-score); AHI-apnea hypopnea index.

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Table 2

Impact of positive airway pressure therapy on sleep symptoms.

	Baseline visit	Follow-up visit	Change	p-value
	mean (SD)/n(%)	mean (SD)/n (%)	mean (SE) /n (%)	
ESS (score/24) (n=104)	8.8 (5.2)	7.3 (4.4)	-1.5 (0.4)	<0.0001
Prevalence of EDS (n=104)	36 (34.6)	21 (20.2)	-15 (14.4)	0.004
PROM-SDA (t-score) (n=107)	54.7 (6.3)	51.0 (6.0)	-3.7 (0.6)	<0.0001
PROM-SRI (t-score) (n=106)	54.3 (9.8)	50.2 (9.7)	-4.1 (1.0)	<0.0001

ESS: Epworth sleepiness scale; EDS: Excessive Daytime Sleepiness. PROM-SDA: Patient Reported Outcome Measure Information System (PROMIS)-Sleep Disturbance instrument (t-score); PROM-SRI Patient Reported Outcome Measure Information System (PROMIS)- Sleep Related Impairment instrument (t-score). Significance of changes in ESS, and PROMIS scores were measured by paired t-test. Significance of changes in the prevalence of EDS was assessed by McNemar's test.

Table 3

Changes in glycated hemoglobin and diabetes medication regimens by group.

Changes in Glycated Hemoglobin	Initiated PAP		Declined PAP		Declined Sleep Study	
	90 days	1 year	90 days	1 year	90 days	1 year
HbA1c (NGSP,%)	0.19 (0.09)	0.20 (0.12)	0.02 (0.14)	0.05 (0.19)	0.17 (0.06)	0.17 (0.07)
HbA1c (IFCC, mmol/mol)	2.1 (1.0)	2.2 (1.3)	0.2 (1.5)	0.5 (2.1)	1.9 (0.7)	1.9 (0.8)
Diabetes Medication Regimen Changes						
Increased, n (%)	–	34 (26.6)	–	19 (29.2)	–	135 (25.7)
Unchanged, n(%)	–	84 (65.6)	–	45 (69.2)	–	367 (69.9)
Decreased, n (%)	–	10 (7.8)	–	1 (1.5)	–	23 (4.4)

HbA1c – change in hemoglobin A1c; All values are presented as mean (standard error of the mean).