

measurement of exhaled carbon monoxide (CO<sub>EXH</sub>) at 1, 2, and 3 months. At each monthly visit, each subject also received a medical examination and behavior group therapy counseling and provided self-assessed ratings of his or her withdrawal symptoms and adverse effects.

Subjects in the two groups did not differ in marital status, age, years of education, gender makeup, and smoking behavior variables that included onset of tobacco use, years of smoking, and Fagerström Test for Nicotine Dependence (Table 1). Other similarities included lifetime consumption of cigarettes, prevalence and types of depressive disorders, and alcohol consumption.

Table 1. Characteristics of Groups

Characteristics	Placebo Group (n=17; 7 males, 10 females)	NAC Group (n=14; 2 males, 12 females)	p Value
Current age, years	51.93±7.022	50.76±11.819	0.748
Years of education	10.86±5.318	9.18±5.040	0.375
Smoking onset age	16.86±2.507	16.18±3.340	0.534
Years of smoking	35.00±7.766	33.29±11.889	0.648
Pack-year	32.64±18.519	31.43±18.369	0.846
FTND	4.50±1.743	4.82±2.186	0.657

Data are mean±standard deviation.

FTND=Fagerström Test for Nicotine Dependence.

Significant decreases in the primary outcomes of daily smoking and CO<sub>EXH</sub> were evident in those receiving NAC (Table 2). Withdrawal symptoms and adverse effects were similar in both groups (data not shown in poster).

Table 2. Effects of NAC and Placebo Treatment on Primary Outcomes

		Cigarettes (No./Day)	p Value	CO <sub>EXH</sub> (ppm)	p Value
<b>NAC</b>	Baseline	20±3	<0.001	21±3	0.003
	12 weeks	9±3		10±3	
<b>Placebo</b>	Baseline	19±3	NS	16±2	NS
	12 weeks	16±2		15±2	

Data are mean±standard deviation.

NAC=N-acetylcysteine; NS=not significant.

Analysis of other variables revealed a significant difference in the Hamilton Depression Rating Scale score, with higher scores at baseline and 12 weeks for those receiving placebo (Table 3).

Table 3. Effect of Treatments on Other Outcome Variables

Variable		T0 (Baseline)	Week 12 (Endpoint)	p Value
HAM-D	Placebo	13.6±4.4	12.1±4.6	0.018
	NAC	12.7±7.1	7.2±6.3	
BMI	Placebo	26.2±6.6	26.4±6.9	0.046
	NAC	27.1±5.0	26.5±5.3	
SBP	Placebo	121.4±23.4	118.9±15.3	0.893
	NAC	128.2±16.7	121.8±13.3	
DBP	Placebo	75.7±12.7	77.1±11.1	0.554
	NAC	75.5±8.2	79.1±5.4	
Sheehan (social)	Placebo	3.7±3.1	2.6±3.6	0.594
	NAC	1.6±2.5	1.0±2.0	
Sheehan (work)	Placebo	2.6±3.2	2.7±3.9	0.092
	NAC	1.7±2.5	0.9±2.1	
Sheehan (family)	Placebo	4.0±3.7	2.9±3.0	0.103
	NAC	1.7±2.5	6.6±1.5	

Data are mean±standard deviation.

BMI=body mass index; DBP=diastolic blood pressure; HAM-D=Hamilton Depression Rating Scale score; SBP=systolic blood pressure; Sheehan=Sheehan Disability Scale.

The results support the potential of NAC as a smoking cessation agent and should serve as a springboard for more clinical trials to substantiate this role of NAC.

## rTMS Improves Generalized Anxiety Disorder Compared With Sham Treatment

Written by Mary Beth Nierengarten

Preliminary data indicate that repetitive transcranial magnetic stimulation (rTMS) is superior to a sham treatment for patients with generalized anxiety disorder (GAD). Gretchen J. Diefenbach, PhD, Institute of Living at Hartford Hospital, Hartford, Connecticut, USA, presented the results of an ongoing randomized controlled trial to assess the efficacy of rTMS versus sham treatment for patients with moderate to severe GAD.

In total, 32 patients were enrolled in the study. All patients were at least 18 years of age, with a principal or a coprincipal diagnosis of moderate to severe GAD. Patients were excluded if they had a brain trauma or a disorder, a



medication change within 3 months of the trial, a serious or unstable medical illness, a substance use disorder within 6 months of the trial, a lifetime diagnosis of select psychological diseases (bipolar disease, developmental disorder, obsessive-compulsive disorder, or psychosis), or current posttraumatic stress disorder; were on medications that increased the risk of seizure due to rTMS; were undergoing concurrent psychotherapy; were too unstable to participate; or had any contraindication to magnetic resonance imaging (MRI).

The patients treated by rTMS were treated with low frequency (1 Hz) to the dorsolateral prefrontal cortex (DLPFC) 5 days a week for 6 weeks, which included 900 pulses per session for 270,000 pulses in total.

The primary outcome was an improvement in anxiety as measured by the Hamilton Anxiety Rating Scale (HAM-A), with a response indicated by 50% more improvement and a remitter indicated by a post score of <8.

Patients were assessed prior to treatment, weekly during treatment, after treatment, and at 3-month follow-up. Adverse events were checked daily during the first week, and weekly thereafter. Functional MRI (fMRI) was performed prior to and after treatment. Preliminary results from fMRI assessments were presented by Assaf and colleagues and showed that there was a significant correlation between symptom changes and changes in neural activation at the right DLPFC, such that symptom improvement was associated with increased neural activation [Assaf MA et al. Presented at the Annual Meeting of the Society of Biological Psychiatry, New York, New York (May 2014)].

Of the 32 patients enrolled, 12 were randomized to active rTMS and 12 to sham. Of these, 7 of 12 in the rTMS group and 8 of 12 in the sham group completed treatment, and 5 and 6, respectively, completed 3-month follow-up.

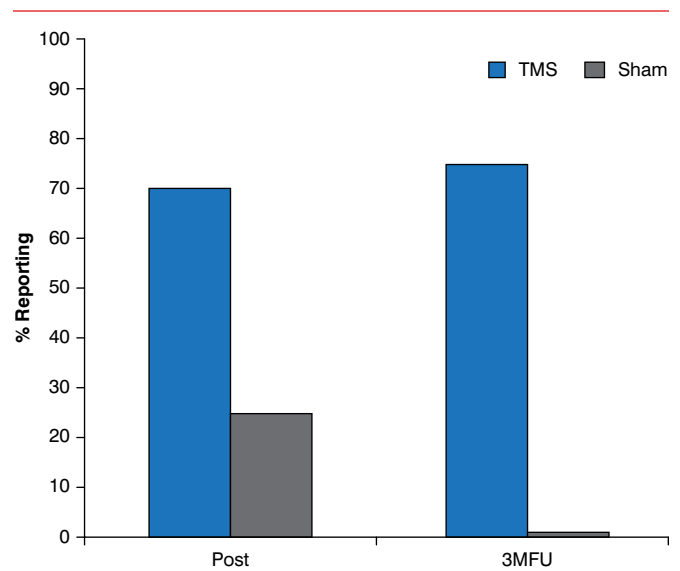
Dr. Diefenbach presented the results on only the patients who completed treatment so far, and she emphasized that the study is ongoing.

Based on the HAM-A scale, the study found that >70% of patients in the TMS group were categorized as responders after treatment compared with 25% in the sham group (Figure 1). At 3-month follow-up, 80% of the rTMS patients and 0% of the sham patients were responders.

The study also found that 43% of the patients in the rTMS group and 13% in the sham group were categorized as remitters after treatment, with 80% and 0%, respectively, considered remitters at 3-month follow-up.

Overall, the incidence of adverse events was similar between the two groups, said Dr. Diefenbach, except for an increased incidence in eye twitch in the rTMS group (Figure 2).

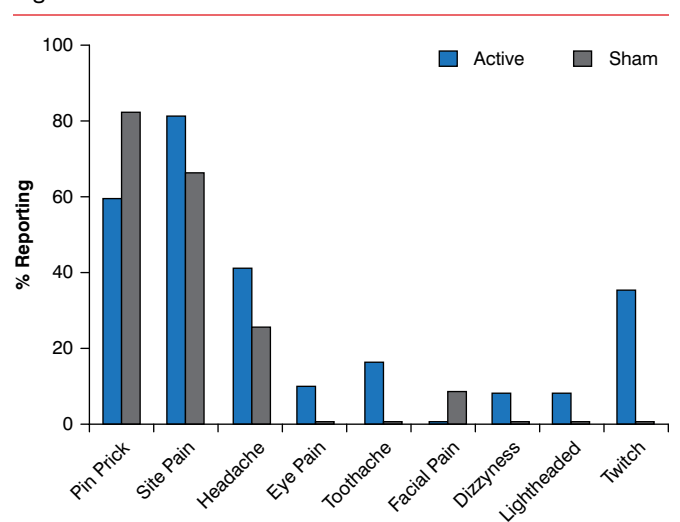
Figure 1. Responders Based on the HAM-A Scale



3MFU=3-month follow-up; HAM-A=Hamilton Anxiety Rating Scale; TMS=transcranial magnetic stimulation.

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Figure 2. Adverse Events



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One serious adverse event occurred in a patient who was hospitalized for chest pain and was diagnosed with coronary vasospasm unrelated to the study procedure or device. No seizures were reported.

Dr. Diefenbach emphasized the importance of further exploring different treatment parameters, saying that one of the main challenges of the trial was the treatment schedule, to which many patients could not commit.