SciMedCentral

Journal of Substance Abuse & Alcoholism

Research Article

Recruitment and Retention of Smokers Versus Nonsmokers in an rTMS Study

Christine E Sheffer[1]*, Sharon Brackman[1], Mark Mennemeier[2], Ginger Brown[2], Reid D Landes[3], John Dornhoffer[4], Timothy Kimbrell[5] and Warren K Bickel[6]

[1]*Department of Health Behavior and Health Education University of Arkansas for Medical Sciences, Little Rock, AR*
[2]*Department of Neurobiology and Developmental Sciences University of Arkansas for Medical Sciences, Little Rock, AR*
[3]*Department of Biostatistics University of Arkansas for Medical Sciences, Little Rock, AR*
[4]*Department of Otolaryngology – Head and Neck Surgery University of Arkansas for Medical Sciences, Little Rock, AR*
[5]*Mental Health Service Central Arkansas Veterans Healthcare System and Department of Psychiatry, University of Arkansas for Medical Sciences, Little Rock, AR*
[6]*Advanced Recovery Research Center Virginia Tech Carilion Research Institute, Roanoke, VA*

***Corresponding author**
Christine E Sheffer, PhD Sophie Davis School of Biomedical Education, City College of New York, Townsend Harris Hall, Suite 400 160, Convent Ave,New York, NY 10031, tel.347-316-0230; Email: csheffer@med.cuny.edu

Submitted: 20 December 2013

Accepted: 07 February 2014

Published: 18 February 2014

Keywords
- Transcranial magnetic stimulation
- Smoking

Abstract

Repetitive transcranial magnetic stimulation (rTMS) is a new frontier in the examination of addictive behaviors and perhaps the development of new interventions. This study examined differences in recruitment, eligibility, and retention among smokers and nonsmokers in an rTMS study. We modeled participant eligibility and study completion among eligible participants accounting for demographic differences between smokers and nonsmokers. Nonsmokers were more likely than smokers to remain eligible for the study after the in-person screen (84.2% versus 57.4%; OR 4.0 CI: 1.0, 15.4, p=0.05) and to complete the study (87.5% versus 59.3%; OR=43.9 CI: 2.8, 687.2, p=0.007). The preliminary findings suggest that careful screening for drugs of abuse and brain abnormalities among smokers prior to administering rTMS is warranted. More research is needed concerning the prevalence of brain abnormalities in smokers. Smokers might need to be informed about a higher risk of incidental MRI findings.

INTRODUCTION

Tobacco dependence is the greatest cause of preventable death and disease in the US today (Department of Health and Human Services [DHHS], 2004). Although 40-60% of smokers make a quit attempt each year, most will relapse within 12 months [1]. New approaches are needed to increase the variety and effectiveness of treatment options [2]. Recent evidence suggests that relapse is influenced by the balance of activity in brain systems involved with decision-making [3-6] and that these systems are affected by neuromodulation of the dorsolateral prefrontal cortex (DLPFC) [7-10] . Neuromodulation has been shown to reduce cigarette consumption among treatment seeking smokers, and in some instances, reduce craving to smoke [11-14]. Repetitive transcranial magnetic stimulation (rTMS) is a noninvasive means of modulating neuronal activity and a novel approach to perhaps developing new interventions for smoking cessation. Nonetheless, rTMS is not a minimal risk procedure and extensive screening processes are often involved which might present a challenge for recruiting and retaining smokers.

As a non-invasive method for altering cortical excitability, rTMS is increasingly being used as an experimental and clinical tool to examine neuroplasticity, alter excitability in specific areas of the brain, and treat a variety of disorders including depression, mania, schizophrenia, obsessive-complusive disorder, panic disorder, posttraumatic stress disorder [15]. rTMS delivered over multiple sessions is now considered a safe and effective treatment for medication resistant depression [16]. The acute effects on neuronal activity are thought to be either excitatory or inhibitory depending on the frequency of the pulses delivered [15,17] although there are exceptions [18]. Low frequency rTMS

(LF; ≤ 3Hz) is believed to inhibit cortical excitability [19,20] and high frequency (HF; >3Hz) to increase cortical excitability [21-24]. Changes in cortical excitability induced by rTMS accumulate in an additive fashion as the number of sessions increases over days.

The primary safety concern with rTMS is inducing seizure, a relatively serious complication; however, the adoption of safety guidelines and screening procedures have made seizure induction a rare occurrence [25-27]. rTMS screening procedures are designed to minimize risk and include an extensive medical history and often, but not always, include neuroimaging. Neuroimaging is also used in stereotaxic systems (e.g., the BrainSight Stereotaxic System, Rogue Research) to precisely locate the area to be stimulated in the brain. Given the extensive screening criteria and the multiple sessions involved with many rTMS studies, some characteristic differences between smokers and nonsmokers might affect the recruitment, eligibility, and retention of participants and thus the generalizability of results.

Neuroimaging studies not associated with rTMS studies suggest that smoking is associated with changes in cortical volume, density, and chemistry [28]. Although changes in cortical volume and density do not necessarily preclude administration of rTMS, these characteristics suggest that there might be other brain abnormalities that in fact do preclude safe administration of rTMS. Smoking also is more common among persons with psychiatric and substance use disorders [29], some of whom might be judged to have an unacceptable risk for adverse events from rTMS for tobacco dependence. A larger proportion of smokers are of lower socioeconomic status (SES; i.e., lower income and lower educational levels) [30], than nonsmokers. Lower SES smokers might experience more barriers to attending multiple sessions of rTMS. Physiologically and a psychologically, smokers also tend to be less healthy than nonsmokers [31].

This study describes the recruitment, screening, enrollment, and retention of smokers and nonsmokers in an rTMS study of decision-making and cigarette consumption [32]. We expected lower SES smokers to be disproportionately represented in the initial among smoking participants and we expected smokers to fail the screening criteria more frequently than nonsmokers due to psychiatric disorders or other substance use. Given that the recruitment and screening procedures were extensive and similar for all participants, we expected to find few differences between smokers and nonsmokers after the initial screening processes, but were aware that attendance might have been affected by SES (i.e., resources).

METHODS

Recruitment and screening

Smokers and nonsmokers were recruited through similar advertisements placed in the same newspapers. All participants underwent extensive telephone screening. If they passed the telephone screening interview, they were invited to an in-person screening visit and explicity informed that they would be expected to pass a urine test for drugs of abuse (cocaine, opiates, amphetamines, benzodiazapines, marijuana, and other drugs of abuse) and a pregnancy test, if applicable, to be eligible to participate. Inclusion criteria included 19-55 years of age, English-speaking, right-handed, and no personal or family history of epilepsy or seizures, no personal history of head injury with unconsciousness, aneurysm, stroke, neurosurgery, psychiatric disorder that required hospitalization, tinnitus, metal implants in head, neck, or cochlea, pacemaker, migraine headaches, medications that lower seizure threshold, and/or claustrophobia. Participants could not be pregnant. Nonsmokers reported no smoking in the past two years. Smokers were required to smoke at least 10 cigarettes per day and have no plans to quit smoking in the next 30 days.

After passing in-person screening, participants were consented, enrolled, and scheduled for a high-resolution MRI of the head. Results of the MRI were used to screen for brain abnormalities that would preclude administration of rTMS and for precisely locating the stimulation site with the BrainSight Stereotaxic System (Rogue Research, Inc.). The MRI was reviewed by a staff radiologist and the study physician and if the results revealed abnormalities that precluded the safe administration of rTMS, participants were withdrawn from the study. Participants with brain abnormalities that did not preclude the administration of rTMS were eligible to continue.

Phase one of the parent study delivered three counterbalanced conditions of high-frequency rTMS to both smokers and nonsmokers (10Hz, 20Hz, and sham). To ensure that smokers were not in withdrawal, smokers were required to smoke one cigarette immediately before beginning session procedures. All stimulation sessions were delivered over the left DLPFC guided by the Brainsight System (Rogue Research, Inc.). Stimulations are separated by at least 48 hours. Participants were paid $25 if they passed the in-person screening, $25 for the MRI visit, and $25 for each session visit. Smokers were provided with two packs of their preferred brand of cigarettes immediately after the visit was complete. With the exception of the MRI visit, payment was made in check immediately after the visit was complete.

Measures

Demographic information included age, sex, race, ethnicity, partnered status (married or living with significant other), household income, educational level, employment status, and type of healthcare insurance. Household income was assessed with six categories utilized by the US Census Bureau (<$10,000, $10,000 to $14,999, $15,000 to $24,999, $25,000 to $34,999, $35,000 to $49,999, ≥$50,000) (Census Bureau, 2000). Educational level was assessed with years of completed education which was grouped into four categories (< 12, 12, 13-14, and ≥ 15 years of education). Educational level and household income were combined into a composite measure of SES as follows: Values of 1 (lowest) to 4 (highest) were assigned to the four categories of education. Values of 1 (lowest) to 6 (highest) were assigned to the six categories of household income. Adding the income and educational level values resulted in a discrete analogue SES scale (range of 2 = lowest to 10= highest) [32].

Analyses

Demographic data were available for all those participants who passed the in-person screen and were enrolled. Analysis of

variance and χ^2 were utilized to examine demographic differences between smokers and nonsmokers and to examine differences between smokers and nonsmokers at each step of the eligibility and retention process.

With smoking status as the variable of interest, logistic regressions were utilized to develop two models: 1) continued participant eligibility once enrolled (i.e., through the MRI screen; eligible, not eligible), and 2) once eligible, completing phase one of the study (three rTMS sessions; completed, not completed). Demographic differences between smokers and nonsmokers were included in the model to account for these differences between smokers and nonsmokers. A backward conditional process eliminated variables with significance levels > 0.10 in a step-wise manner. All demographic variables found to differ significantly by smoking status were included in the models. Significance was set at $\alpha = 0.05$.

Table 1: Differences between smokers and nonsmokers.

Differences between smokers and nonsmokers				
		Smoker (n=19)	Non-smoker (n=47)	p-value
Age (mean, SD)		42.4 (10.0)	39.2 (11.2)	0.26
Male (percent, n)		70.2 (33)	36.8 (7)	0.01
Race (percent, n)				0.22
	White	63.8 (30)	89.5 (17)	
	African American	31.9 (15)	10.5 (2)	
	American Indian	2.1 (1)	0 (0)	
	Other	2.1 (1)	0 (0)	
Hispanic (percent, n)		2.1(1)	0 (0)	0.52
Partnered (percent, n)		30.4 (14)	36.8 (7)	0.62
Household income (percent, n)				0.04
	<$10,000	42.6 (20)	10.5 (2)	
	$10-14,999	12.8 (6)	5.3 (1)	
	$15-24,999	19.1 (9)	15.8 (3)	
	$25-34,999	6.4 (3)	21.1 (4)	
	$35-49,999	6.4 (3)	15.8 (3)	
	≥$50,000	12.8 (6)	31.6 (6)	
Educational level (mean, SD)		12.7 (1.9)	15.4 (2.0)	<0.0001
Educational level (percent, n)				<0.0001
	< 12 years	19.1 (9)	5.3 (1)	
	12 years	42.6 (20)	5.3 (1)	
	13-14 years	23.4 (11)	15.8 (3)	
	≥ 15 years	14.9 (7)	73.7 (14)	
Socioeconomic status (mean, SD)*		4.9 (2.5)	7.8 (2.2)	<0.0001
Employment status (percent, n)				0.13
	Full-time	25.5 (12)	52.6 (10)	
	Part-time	23.4 (11)	26.3 (5)	
	Retired	2.1 (1)	0 (0)	
	Disabled	2.1 (1)	0 (0)	
	Unemployed	44.7 (21)	15.8 (3)	
	Homemaker	2.1 (1)	0 (0)	
	Student	0 (0)	5.3 (1)	
Healthcare insurance type (percent, n)				<0.0001
	Private	23.4 (11)	78.9 (15)	
	Medicare	2.1 (1)	0 (0)	
	None	74.5 (35)	21.1 (4)	

*Socioeconomic status was a composite score comprised of educational level and household income (range of 2 = lowest to 10= highest)

RESULTS

Participants who passed the in-person screen (n=66) were 60.6% male with a mean age 41.5 (SD 10.4) years; they were 71.2% white, 25.8% African-American, and 3% American Indian or other; 98.5% non-Hispanic; and 32.3% partnered. They had a mean of 13.5 (SD 2.3) years of education; 57.5% were employed full- or part-time, 36.4% unemployed, and 6.0% retired, disabled, homemakers, or students. About two-thirds of participants (62.1%) reported household incomes less than $25,000; 39.4% had private health insurance; 59.1% had no health insurance, and 1.5% had Medicare.

Differences between smokers and nonsmokers were found for sex, household income, educational level, and health insurance status. See Table 1. Smokers were more likely to be male than nonsmokers (70.2% versus 36.8%; $\chi^2 = 6.3$, df = 1, p=0.01). Smokers were generally of lower SES than nonsmokers, M=4.9 (SD 2.5) versus M=7.8 (SD 2.2), F (1,65)=19.26, p<0.0001. Smokers were more likely to have no health insurance than nonsmokers (74.5% versus 21.1%; $\chi^2 = 17.5$, df = 2, p < 0.0001). Differences between smokers and nonsmokers occurred at nearly every step in the recruitment and retention process. See Table 2. Statistically significant differences in participant attrition occurred during the in-person screening where more smokers failed the urine drug screen than nonsmokers (38.7% versus 9.5%; χ^2=6.4, df = 1, p=0.01) even though all potential participants were informed during the telephone screening interview that they would be given a urine drug test and that eligibility was contingent upon passing the drug screen. Although significance did not reach .05, more brain abnormalities that precluded rTMS were found among smokers than nonsmokers (18.2% versus 0%; χ^2 =3.3, df = 1, p=0.07). These abnormalities included evidence of stroke (ischemic and infarct), multiple sclerosis, and past injury as well as a notable cyst and an aneurysm. A brain abnormality that did not preclude rTMS, a hemangioma, was found in one other smoker. Follow-up analysis of variance determined that the mean age of participants with abnormalities was no different from the mean age of those without abnormalities (44.5 years versus 41.1 years; F (1, 47) = .48, p=0.49).

The logistic regression models of eligibility and completing phase one of the study included sex, SES, and healthcare insurance status to account for differences between smoker and nonsmokers. Because the SES composite score included household income and educational level, the SES composite score was included in lieu of the educational and household incomes variables individually. Smoking status was the only variable that remained in the model of eligibility. Of those who were passed the in-person screening interview and were enrolled, nonsmokers were significantly more likely than smokers to remain eligible for the study (84.2% versus 57.4%; OR=4.0 CI: 1.0, 15.4, p=0.05). The model for completing phase one of the study retained three variables: sex, healthcare insurance status, and smoking status. Smoking status was the only statistically significant variable. Of those that were finally eligible for the study (n=43), nonsmokers were significantly more likely than smokers to complete phase one of the study (87.5% versus 59.3%; OR=43.9 CI: 2.8, 687.2, p=0.007); women were more likely to complete the study than men (63.2% versus 75.0%; OR=0.2 CI: 0, 1.0, p=0.06); those with

Table 2: Retention of smokers and nonsmokers throughout the recruitment and eligibility process.

		n=545 Screened by telephone		
	Smokers n=137	Scheduled for in-person screen	Nonsmokers n=34	
Retained 55% of those scheduled	n=75	Attended in-person screening (p=0.46)	n=21	Retained 62% of those scheduled
Retained 63% of attendees / 34% of scheduled	n=47	Passed in-person screening and enrolled* (p=0.02)	n=19	Retained 90% of attendees/ 56% of scheduled
Retained 70% of those who passed in-person screen / 24% of scheduled	n=33	Obtained MRI (p=0.29)	n=16	Retained 84% of those who passed in-person screen / 47% of scheduled
Retained 82% of those who obtained MRI / 20% of scheduled	n=27	Passed MRI screen. Final eligibility** (p=0.07)	n=16	Retained 100% of those who obtained MRI / 47% of scheduled
Retained 85% of those who passed the MRI screen / 16% of scheduled	n=23	Completed at least one rTMS session (p=0.11)	n=16	Retained 100% of those who passed the MRI screen / 47% of scheduled
Phase One Retained 70% of those who attended at least one session / 12% of scheduled	n=16	Completed at least three rTMS sessions (p.0.55)	n=14	Phase One Retained 88% of those who attended at least one session / 41% of scheduled

*In-person screen failures due to failing drug test; **MRI screen failures were due to abnormal findings in MRI that precluded safe administration of rTMS; rTMS = repetitive transcranial magnetic stimulation.

no insurance were more likely to complete the study than those with private insurance (72.0% versus 66.7%; OR= 6.8 CI:0.9, 53.7).

DISCUSSION

These findings indicate that recruiting and retaining smokers for an rTMS study entails some particular challenges. The primary challenges were related to screening for safety concerns. Secondary concerns were related to attrition during and after the screening processes. These findings have broad implications for researchers and clinicians.

More smokers than nonsmokers possessed characteristics that raised safety concerns for the delivery of rTMS. Although the relatively high frequency of smokers who tested positive for drugs of abuse even after being informed of the required drug screen is curious, the prevalence of smoking is 2-3 times higher among substance users than the general population so perhaps this finding is unsurprising [29]. Of particular concern to us was our finding that smokers presented with a higher frequency of brain abnormalities. Recent meta-analyses suggest that the prevalence of incidental findings from high-resolution MRI is about 4.3%, but no studies to date stratify participants with incidental findings by smoking status [33]. In our study, the prevalence of significant incidental brain abnormalities was 12.2%. The rate for smokers was 37.5% compared with nonsmokers whose rate was 0%. Although this difference was not statistically significant (p=0.07), this study was not powered to detect this difference and the possibility exists that these results reflect a Type II error and/or these findings indicate a significant trend. Additional research is needed to determine if all smokers should be tested for drugs of abuse prior to administration of rTMS. Additional research is also needed to determine if brain abnormalities that preclude rTMS administration indeed occur at a higher prevalence in smokers. If so, this would have significant implication for smokers seeking rTMS treatment for any disorder.

The prevalence of the incidental brain abnormalities in this study warrants caution in the development of rTMS clinical and study procedures that include smokers. Specific procedures are needed to manage incidental findings from MRIs for rTMS studies especially if MRIs become indicated for all smokers who plan to undergo rTMS. Learning about a brain abnormality can be distressing, especially if the prognosis is unclear and the risks associated with intervention are high [26,33]. For example, discovering an aneurysm is likely to require close monitoring and perhaps an intervention with significant risk. Awareness of the condition might affect many aspects of an individual's life [33]. While it is often necessary and prudent to screen rTMS participants for brain abnormalities using MRI, and brain imaging is necessary to assist in finely targeted rTMS delivery, participants must be fully informed of the risks of the incidental discovery of a brain abnormalities and researchers and clinicians must have a plan in place to refer participants for follow up care.

Although we accounted for demographic differences, the cumulative difference between smokers and nonsmokers in retention after screening remained significant. We speculate that statistically accounting for SES even with a composite measure, which is generally a more powerful measure of SES than singular measures [34] was not enough to account for the differences in resources between smokers and nonsmokers and that there are clearly other characteristics that we did not account for that

contributed to this difference such as perhaps cognitive and/or emotional resources.

The differences between smokers and nonsmokers throughout the recruitment, eligibility, and retention process indicates that smokers are more challenging to recruit and retain in rTMS studies. While the reasons for the losses in retention at nearly every step in the process are sometimes unclear, the cumulative effects had a dramatic impact on recruitment efforts. This finding indicates that enhanced recruitment and retention strategies for smokers should be in place for rTMS studies that recruit smokers. This also suggests that there might be differences between smokers and nonsmokers that were not assessed in this study, but can affect the comparability of the two groups.

Limitations of this off-project study include a small number of participants, increasing the possibility of Type II errors. This study was also limited by the few baseline characteristics that we were able to utilize to examine differences between smokers and nonsmokers, reducing our ability to more fully examine factors that contributed to different recruitment and eligibility outcomes. Additionally, the differences between smokers and nonsmokers in this study might have been amplified because we only recruited smokers with no plans to quit in the next 30 days.

FUNDING

This research is supported by awards from the National Center for Research Resources (P20 RR20146, 1UL1RR029884) and the National Institute of Child Health and Human Development (HD055677, HD055269).

FINANCIAL DISCLOSURES

Dr. Sheffer has received research funding from Pfizer, Inc. Dr. Bickel is a principal in HealthSIm LLC. Drs. Mennemeier, Dornhoffer, Landes, and Kimbrell, and Ms. Brackman, and Brown reported no biomedical financial interests or potential conflicts of interest.

REFERENCES

1. Hughes JR, Gulliver SB, Fenwick JW, Valliere WA, Cruser K, Pepper S, et al. Smoking cessation among self-quitters. Health Psychol. 1992; 11: 331-334.
2. Fiore, M.C., Jaén, C.R., Baker, T.B., Bailey, W.C. , Benowitz, N.L., Curry, S.J., . . . Wewers, M.E. (2008). Treating tobacco use and dependence: 2008 update. Clinical Practice Guideline. Rockville, MD: Public Health Service.
3. Bickel, W. K., & Yi, R. Temporal discounting as a measure of executive function: insights from the competing neuro-behavioral decision system hypothesis of addiction. Advances Health Economics and Health Services Research. 2008; 20:289-309.
4. McClure S. M, Laibson D. I, Loewenstein G, & Cohen J. D. Separate neural systems value immediate and delayed monetary rewards. Science. 2004; 306: 503-507.
5. Nestler EJ, Landsman D . Learning about addiction from the genome. Nature. 2001; 409: 834-835.
6. Verdejo-Garcia A, Lopez-Torrecillas F, Gimenez C. O, & Perez-Garcia M. Clinical implications and methodological challenges in the study of the neuropsychological correlates of cannabis, stimulant, and opioid abuse. Neuropsychological Review. 2004; 14: 1-41.
7. Fecteau S, Knoch D, Fregni F, Sultani N, Boggio P, & Pascual-Leone A. Diminishing risk-taking behavior by modulating activity in the prefrontal cortex: a direct current stimulation study. Journal of Neuroscience. 2007; 27: 12500-12505.
8. Fecteau, S., Pascual-Leone, A., Zald, D. H., Liguori, P., Theoret, H., Boggio, P. S., & Fregni, F. Activation of prefrontal cortex by transcranial direct current stimulation reduces appetite for risk during ambiguous decision making. Journal of Neuroscience. 2007; 27: 6212-6218.
9. Knoch D, Fehr E . Resisting the power of temptations: the right prefrontal cortex and self-control. Ann N Y Acad Sci. 2007; 1104: 123-134.
10. Sheffer, C, Stitzer, M., Brackman, S., Moore, P., & Munn, T. Socioeconomic disparities in community-based treatment of tobacco dependence. American Journal of Public Health, ePub ahead of print January 19, 2012.
11. Amiaz R, Levy D, Vainiger D, Grunhaus L, Zangen A . Repeated high-frequency transcranial magnetic stimulation over the dorsolateral prefrontal cortex reduces cigarette craving and consumption. Addiction. 2009; 104: 653-660.
12. Eichhammer P, Johann M, Kharraz A, Binder H, Pittrow D, Wodarz N, & Hajak G. High-frequency repetitive transcranial magnetic stimulation decreases cigarette smoking. Journal of Clinical Psychiatry. ;2003 64: 951-953.
13. Johann M, Wiegand R, Kharraz A, Bobbe G, Sommer G, Hajak G, et al Repetitiv Transcranial Magnetic Stimulation in Nicotine Dependence. Psychiatr Prax. 2003; 30:129-131.
14. Wing V. C, Bacher I, Wu B. S, Daskalakis Z. J, & George T. P. High frequency repetitive transcranial magnetic stimulation reduces tobacco craving in schizophrenia. Letter Randomized Controlled Trial Research Support, Non-U.S. Gov't. Schizophr Res. 2012; 139: 264-266.
15. George M. S, Padberg F, Schlaepfer T. E, O'Reardon J. P, Fitzgerald P. B, Nahas Z. H, et al. Controversy: Repetitive transcranial magnetic stimulation or transcranial direct current stimulation shows efficacy in treating psychiatric diseases (depression, mania, schizophrenia, obsessive-compulsive disorder, panic, posttraumatic stress disorder). Brain Stimulation. 2009; 2: 14-21.
16. O'Reardon J. P, Solvason H B, Janicak P. G, Sampson S, Isenberg K. E, Nahas, Z, et al. Sackeim, H. A. Efficacy and safety of transcranial magnetic stimulation in the acute treatment of major depression: a multisite randomized controlled trial. Biological Psychiatry, 2007; 62: 1208-1216.
17. Di Lazzaro, V, Pilato F, Saturno E, Oliviero A, Dileone M, Mazzone P, et al Theta-burst repetitive transcranial magnetic stimulation suppresses specific excitatory circuits in the human motor cortex. The Journal of Physiology, 2005; 565: 945-950.
18. Fitzgerald PB, Fountain S, Daskalakis ZJ . A comprehensive review of the effects of rTMS on motor cortical excitability and inhibition. Clin Neurophysiol. 2006; 117: 2584-2596.
19. Bear MF . Homosynaptic long-term depression: a mechanism for memory? Proc Natl Acad Sci U S A. 1999; 96: 9457-9458.
20. Stanton PK, Sejnowski TJ . Associative long-term depression in the hippocampus induced by hebbian covariance. Nature. 1989; 339: 215-218.
21. Chen R, Classen J, Gerloff C, Celnik P, Wassermann EM, Hallett M, Cohen LG . Depression of motor cortex excitability by low-frequency transcranial magnetic stimulation. Neurology. 1997; 48: 1398-1403.
22. Malenka RC, Nicoll RA . Long-term potentiation--a decade of progress? Science. 1999; 285: 1870-1874.

23. Pascual-Leone, A., Tormos, J. M., Keenan, J., Tarazona, F., Canete, C., & Catala, M. D. Study and modulation of human cortical excitability with transcranial magnetic stimulation. Journal of Clinincal Neurophysiology, 1998; 15:333-343.

24. Wu T, Sommer M, Tergau F, Paulus W . Lasting influence of repetitive transcranial magnetic stimulation on intracortical excitability in human subjects. Neurosci Lett. 2000; 287: 37-40.

25. Rossi, S., Hallett, M., Rossini, P. M., & Pascual-Leone, A. Safety, ethical considerations, and application guidelines for the use of transcranial magnetic stimulation in clinical practice and research. Clin Neurophysiol, 2009; 120: 2008-2039.

26. Wassermann, E. M. Safety and side-effects of transcranial magnetic stimulation and repetitive transcranial magnetic stimulation. New York: Arnold Publishers. (2002).

27. Wassermann EM, Cohen LG, Flitman SS, Chen R, Hallett M . Seizures in healthy people with repeated "safe" trains of transcranial magnetic stimuli. Lancet. 1996; 347: 825-826.

28. Domino EF . Tobacco smoking and MRI/MRS brain abnormalities compared to nonsmokers. Prog Neuropsychopharmacol Biol Psychiatry. 2008; 32: 1778-1781.

29. Kalman D, Morissette SB, George TP . Co-morbidity of smoking in patients with psychiatric and substance use disorders. Am J Addict. 2005; 14: 106-123.

30. Centers for Disease Control and Prevention. (2010). Behavioral risk factor surveillance system survey data. Atlanta: US Department of Health and Human Services, Centers for Disease Control and Prevention. Retrieved from http://apps.nccd.cdc.gov/BRFSS/income.asp?cat=TU&yr=2010&qkey=4396&state=US

31. Department of Health and Human Services [DHHS]. (2004). The health consequences of smoking: A report of the Surgeon General. Atlanta, GA: Department of Health and Human Services, Centers for Disease Control and Prevention.

32. Sheffer CE, Mennemeier M, Landes RD, Bickel WK, Brackman S, Dornhoffer J, Kimbrell T . Neuromodulation of delay discounting, the reflection effect, and cigarette consumption. J Subst Abuse Treat. 2013; 45: 206-214.

33. Morris Z, Whiteley WN, Longstreth WT Jr, Weber F, Lee YC, Tsushima Y, Alphs H . Incidental findings on brain magnetic resonance imaging: systematic review and meta-analysis. BMJ. 2009; 339: b3016.

34. Galobardes B, Shaw M, Lawlor DA, Lynch JW, Davey Smith G . Indicators of socioeconomic position (part 2). J Epidemiol Community Health. 2006; 60: 95-101.

Cite this article

Sheffer CE, Brackman S, Mennemeier M, Brown G, Landes RD, et al. (2014) Recruitment and Retention of Smokers Versus Nonsmokers in an rTMS Study. J Subst Abuse Alcohol 2(3): 1019.