# Transcranial Doppler in Smoking Relapse Prevention Strategy

## N. Blažić-Čop, V. Šerić, V. Bašić, N. Thaller and V. Demarin

Department of Neurology, University Hospital »Sestre milosrdnice», Zagreb, Croatia

# ABSTRACT

Nicotine dependence is a progressive, chronic, relapsing disorder. Nicotine is the principal and most potent psychopharmacologically active component of tobacco smoke. Through activation of nicotine receptors in the central nervous system, nicotine can lead to tolerance and dependence. Cessation of smoking is followed by severe pathophysiologic withdrawal and by long-term craving. TCD measurement of cerebral blood flow velocity (BFV) and nicotine dependence degree measured by Fragestrom questionnaire was analyzed in relation to smoking relapse. This study includes 47 participants (25 females and 22 males) included in Breathe Free Plan To Stop Smoking in Non Smoking School in Zagreb.12 month following the end of treatment participants were divided in three groups: continued abstinence, interrupted abstinence and non abstinence. High nicotine dependence combined with TCD pathological finding significantly discriminated successes and failures, suggesting that smokers with pathological TCD need specific therapeutic approach with more social support, individualized coping skills and cognitive restructuring. Measuring cerebral flow velocity by transcranial Doppler in smokers showed the practical validity in prediction of smoking relapse.

#### Introduction

Nicotine dependence is a progressive, chronic, relapsing disorder. The absorption of nicotine by the blood is very rapid. Nicotine is quickly distributed to the brain and its effects on the central nervous system are manifested almost instantaneously<sup>1</sup>. Through activation of nicotine receptors in the central nervous system, nicotine can lead to tolerance and physiological dependence. Nicotine modulates neural and neuroendocrine activity in a variety of loci, including the sympathetic nervous system, the hypothalamic-pituitary-adrenocortical axis, and endogenous opioid systems. It is also known to stimulate vasopresin release.

Cigarette smoking is directly related to the extent of atherosclerotic disease involving large and small arteries in the brain and makes a significant independent contribution to the risk of stroke,

Received for publication June 16, 2000.

which increases with the number of cigarettes  $smoked^{2-5}$ .

Most smokers find it difficult to stop smoking, even after they have made a conscious decision to do so. A number of studies have shown that the majority can achieve only short-term abstinence. The length of abstinence for 66% of individuals is less than 3 months<sup>7</sup>.

Two main factors determine whether or not an individual smoker stop smoking: motivation (level of motivation) and addiction (degree of addiction). There are many successful methods how to help people quit smoking. They usually include basic health education, discussion of withdrawal symptoms, strategies to prevent relapse, group support, stress management, nutrition, exercise and sometimes pharmacological aids<sup>8</sup>. Maintenance of abstinence is influenced by number of interrelated factors and smoking relapse remains serious problem that merits research attention.

High risk situations most commonly associated with relapse as negative emotional stress (loneliness, sadness, grief, anger, frustration), interpersonal conflicts and social pressure are well known<sup>9</sup>. The absence or inadequacy of coping in relapse crises has been identified as a contributor to relapse<sup>10</sup>. Understanding the relationship between stress and smoking would help to clarify the role of stress in relapse<sup>11,12</sup>. Mermelstein et al. in their study of stress and social support founded that high perceived stress posttreatment was associated with relapse but that pretreatment stress had no predictive value.

In multiple risk factor intervention trial (MRFIT) social support and number of cigarettes smoked at baseline significantly discriminated between successes and recidivists.

The prevalence of relapse increases with the high score on Fragestrom Questionnaire<sup>13,14</sup>. The degree of nicotine dependence is an important predictor of both short term and long term treatment outcome. Determining the degree of nicotine dependence may help select the optimal mode of therapy. Repeated relapse is expected in smokers who are heavily dependent on nicotine. They need special programs with specific characteristics: accessibility, comprehensiveness, skillbuilding and support. People who are more dependent on nicotine benefit most from nicotine replacement therapy. Cessation programs must address all stages of the cessation process<sup>1</sup>.

The aim of our investigation was to determine the predisposition or vulnerability to relapse in ex smokers, using TCD measurement of blood flow velocity and nicotine dependence degree by Fragestrom questionnaire.

## **Patients and Methods**

We examined 47 participants who were included in Breathe Free Plan to Stop Smoking in Non-smoking school in Zagreb. There were 25 female (53%) and 22 males (47%), aged 26 to 61. The mean age was 39.2.

The smoking cessation program lasted five days and consisted of five consecutive 2 hours sessions with fallow up support during one year.

The Fragestrom questionnaire was used to identify the degree of nicotine dependency. A score 1–6 indicates a low dependency. A score 7–11 indicates high dependency.

Transcranial color Doppler was performed by use of a pulsed wave Doppler ultrasound device 3D TCD scanner, with a 2 MHz probe. Data were analyzed according to blood flow velocity (BFV) changes. Results were categorized as increased circulatory resistance (CR), decreased CR and normal CR depending on side changes and symmetry. Smoking status of participants was evaluated 12 month following the end of treatment in Non smoking school.

According to self-reported smoking status participants were divided in three groups: continued abstinence, interrupted abstinence and non-abstinence (return to baseline smoking).

Date have been analyzed by  $^2$  - test and variance analysis (ANOVA), and p < 0.005 was considered as level of statistical significance.

## Results

Most smokers need more than one quit attempt to succeed in quitting. In our study 19 (40%) participants who attended smoking cessation program (Breathe Free Plan to Stop Smoking) obtained abstinence after one or more relapses, 12 (26%) participants returned on baseline smoking and only 16 (34%) participants reported continuous abstinence one year after treatment.

Analysis of intracranial artery circulatory changes has shown that only 18 (38 %) had normal TCD finding. Correlation between TCD finding and analyzed variables (age, sex, cigarette smoked per day, years of smoking, degree of nicotine dependency, smoking status one year after treatment) is shown in the Table 1.

 TABLE 1

 CORRELATION BETWEEN TCD FINDING AND

 ANALYZED VARIABLES

	2	р
Age > 50 years	3.9	< 0.048
Sex	1.36	< 0.23
Cigarettes / day	5.76	< 0.017
Years of smoking	4.0	< 0.26
Nicotine dependency	24.6	< 0.001
Smoking status	18.0	< 0.001

The most participants who relapsed and returned on baseline smoking, smoked over 20 years (Figure 1). There was no significant difference between daily smoked cigarettes in all three groups of participants (divided according to self-reported smoking status) (Figure 2).

Smoking time duration

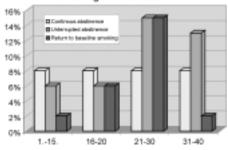


Fig. 1. Smoking status one year after treatment in relation to smoking time duration.  $^{2} = 5.3; p < 0.5.$ 

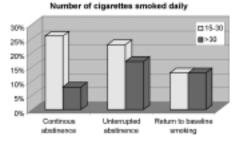


Fig. 2. Daily smoked cigarettes in relation to smoking status of participants one year after treatment in Non-smoking school.  $^{2} = 2.0; p < 0.3.$ 

Among participants high dependent on nicotine 26% returned on baseline smoking and (30%) had one or more relapses (Figure 3). High dependent ex smokers had also higher percent of pathological TCD findings, than those low dependent on nicotine (Figure 4). Most of participants with normal TCD finding were successful and obtained continuous abstinence one year after treatment in Non smoking school in Zagreb (Figure 5).

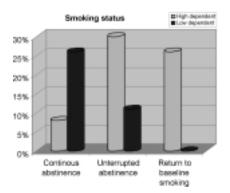


Fig. 3. Nicotine dependency in relation to smoking status of participants one year after treatment in Non-smoking school.  $^2 = 18; p < 0.001.$ 

#### Discussion

TCD findings and degree of nicotine dependency were examined in relation to smoking relapse. It is found that TCD measurement of cerebral flow velocity (BFV) and measurement of nicotine dependency degree by Fragestrom questionnaire are useful methods to determine ex smoker with predisposition or vulnerability to relapse. High nicotine dependency combined with TCD pathological findings significantly discriminated between successes and failures<sup>15</sup>. Relapse is not a failure. Smokers need to know this. Most smokers need more than one quit attempt to succeed. Most relapses occur in the first 3 months after quitting. In process of smoking cessation and maintenance of abstinence biological and psychological factors are inseparable and operate concurrently.

Many situations (parties, finishing a meal, stressful experiences) negative emotions and social pressure may accentuate craving for a cigarette. Ex smokers with pathological TCD findings need specific therapeutic approach with more social support, individualized coping skills and cognitive reconstructing (changing

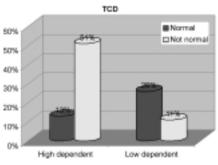


Fig. 4. TCD findings and nicotine dependency.  $\chi^2 = 24,6$ ; p < 0.001.

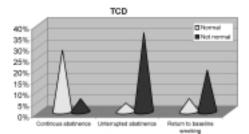


Fig. 5. TCD finding and smoking status of participants one year after treatment in Non-smoking school.  $^2 = 38$ ; p < 0.001.

attitudes and self perceptions related to smoking behavior).

The results of our investigation suggest that it is possible to predict which participants in a smoking cessation program will have problems with cessation and maintenance of cessation and that program can target intervention toward specific individual needs.

Measuring cerebral blood flow velocity by TCD showed the practical validity in prediction of smoking relapse<sup>16,17,22–25</sup>.

Cessation of smoking is followed by severe pathophysiologic withdrawal and by long-term craving. The classic nicotine withdrawal symptoms (dysphoric or depressed mood, insomnia, irritability, frustration or anger, anxiety, concentration difficulties, restlessness and decreased heart rate usually last some days or perhaps weeks<sup>18</sup> and generally are consistent with the pharmaco-kinetics of the metabolism and elimination of nicotine and its metabolites.

Craving for nicotine may persist for months or even years, stimulated by cues associated with smoking – persons, places, situations and sensations including the sight of cigarettes and the smell and taste of tobacco. Recent data indicate that the majority of individuals can achieve only short-term cessation. Up to 80 smokers who initially succeed stop smoking will relapse over a 12-month follow up period<sup>7</sup>. The commonest reasons to give up smoking are health (87%), expense (51%) and family pressure (43%).

There are many successful methods how to help people quit smoking. They usually include basic health education, discussion of withdrawal symptoms, strategies to prevent relapse, group support, stress management, nutrition, exercise and sometimes pharmacological aids (nicotine replacement therapy, Bupropion). Maintenance of abstinence is influenced by number of interrelated factors and smoking relapse remains serious problem that merits research attention.

Although many biological effects of tobacco use and cessation are well known, the role of these factors in smoking relapse has to be clarifyed<sup>18</sup>.

Benfart and Eaker founded that lighter smokers had a much higher quit rate and were able to translate the wish to quit into a decision to quit.

Persons who were more physiologically reactive to stress were more likely to relapse than were their less reactive counterparts. Smokers high in negative affect were more likely to relapse<sup>19</sup>.

The younger age at which individuals take up smoking, the more likely it is that they will continue to smoke throughout their lives  $^{20}$ . About 90% of adult smokers take up smoking as children and adolescents.

The technology of abstinence verification has developed rapidly in the past ten years. Expired air carbon monoxide is useful only for detecting smoking in the 24 hr preceding the test. Blood cotinine is most useful for detecting nicotine use in the 48 hr before the test. Current solutions for assessment of continuous abstinence for longer duration are not entirely satisfactory. Thiocyanate detects smoking from 10 days to 14 days after smoking cessation but measurement of thiocyanat from body fluids can be contaminated by diet (broccoli, cabbage) and light smoking may not be detected. Improved measures for verifying long-term abstinence need to be developed.

Because of the limitations of biological assessment we accepted a self-report of abstinence.

Approximately 60 percent of adult smokers have made at least one serious attempt to give up cigarette, but have relapsed<sup>21,22</sup>. There are varieties of reasons why smokers relapse. TCD as noninvasive diagnostic procedure as well as measurement of nicotine dependence degree by Fragestrom questionnaire is recognized to play an important role in planning of maintenance treatment. Also, it is important that CBF measurement by TCD has high reproducibility, because the values are standardized. The high-risk smokers need specific cessation and maintestrategies. Our investigation nance should encourage physicians to integrate in daily practice many kinds of specific cessation and maintenance strategies.

In our investigation was shown also, that throughout life style changes, the participants with hypertension were very successful in controlling their high blood pressure.

#### Conclusions

TCD findings and degree of nicotine dependency were examined in relation to smoking relapse. It is found that TCD measurement of cerebral blood flow velocity (BFV) and measurement of nicotine dependence degree by Fragestrom questionnaire are useful methods to determine ex smoker s predisposition or vulnerability to relapse. High nicotine dependency combined with TCD pathological findings significantly discriminated between successes and failures. Biological and psychological factors are unseparable and operate concurrently. Many situations (parties, finishing a meal, stressful experiences) negative emotions and social pressure may accentuate craving for a cigarette. Ex smokers with pathological TCD findings need specific therapeutic approach with more social support, individualized coping skills and cognitive restructuring (changing attitudes and self perceptions related to smoking behavior).

The results of our investigation suggest that it is possible to predict which participants in a smoking cessation program will have problems with cessation and maintenance of abstinence and that program can target intervention toward specific individual needs.

Measuring cerebral blood flow velocity by transcranial doppler showed the practical validity in prediction of smoking relapse.

### REFERENCES

1. GRASSI, G., G. SERAVALLE D. A. CAL-HOUD, Circulation, 90 (1994) 248. - 2. SHEFFER, E., E. WESTE, J. WOEHRLE, Clin. Invest., 70 (1992) 149. — 3. TELL, G. S., G. HOWARD, J. A. M. A., 17 (1982) 129. – 4. BLAŽIĆ -ČOP, N., V. HUDOLIN, Mediterranean J. Soc. Psych., 2 (1981) 87. - 5. SU, C., Pharamacol. Ther., 17 (1982) 129. - 6. LIPKUS, I. M., J. C. BAREFOOT, R. B. WILLIAMS, I. C. SIEG-LER, Health Psychol., 13 (1994) 149. - 7. HUNT, W. A., D. A. BEASPALEC, J. Clin. Psychiol., 30 (1974) 431. - 8. SHIFFMAN, S., M. E. JARVIK, Psychopharmacologia, 50 (1976) 35. - 9. SCHWARTZ, J., J. A. M. A., 261 (1987) 61. - 10. BROWNELL, K. D., G. A. MARLATT, E. LICHTENSTEIN, G. T. WILSON, Am. Psychol., 41 (1986) 765. - 11. PARROT, A., Addict. Behav., 18 (1993) 389. - 12. LESHNER, A., Hosp. Pract., 4 (1996) 47. - 13. DEMARIN, V., N. BLAŽIĆ-ČOP, V. ĐORĐEVIĆ, M. BOŠNJAK, T. RUNDEK, V. POSAVEC, Arteries et Veines, 10 (1991)

N. Blažić–Čop

113. — 14. FRAGESTROM, K. O., Psychology, 32 (1983) 29. - 15. HAXBY, D. G., Am. J. Health Syst. Pharm., 52 (1995) 265. - 16. HODEK-DEMARIN, V., Excerpta Medica, 3 (1981) 470. — 17. WOLF, P. A., R. B. AGOSTINO, J. A. M. A., 259 (1988) 1025. - 18. CONROE, J. H., Ann. N. Y. Acad. Sci., 90 (1960) 48. - 19. POMERLEAU, O., A. COLLINS, S. J. SCIHF-MAN., Consult. Clin. Psychol., 61 (1993) 723. - 20. KENFORD, S. L., M. C. FIORE, D. E. JORENBY, S. S. SMITH, D. WETTER, T. B. BAKER, J. A. M. A., 271 (1994) 589. - 21. FRAGESTROM, K. O., Addict. Behav., 3 (1978) 235. — 22. MARTINIĆ POPOVIĆ, I., Acta Clin. Croat., 37 (1998) 81. — 23. DEMARIN, V., RUNDEK, N. THALLER, S. PODOBт NIK-ŠARKANJI, Acta Clin. Croat., 31 (1992) 3. - 24. LOVRENČIĆ-HUZJAN, A., V. DEMARIN, M. BOSNAR, V. VUKOVIĆ, S. PODOBNIK-ŠARKANJI, Coll. Antropol., 23 (1999) 175. - 25. ALEXANDROV, A. V., V. DEMARIN, Acta Clin. Croat., 38 (1999) 97.

Department of Neurology, University Hospital »Sestre milosrdnice«, Vinogradska c. 29, 10000 Zagreb, Croatia

# TRANSKRANIJSKI DOPLER U STRATEGIJI PREVENCIJE RECIDIVA PUŠENJA

# SAŽETAK

Ovisnost o nikotinu je kronični, progresivni poremećaj. Nikotin je glavni, s farmakološkog aspekta najvažniji aktivni sastojak duhanskog dima. Aktivacijom brojnih nikotinskih receptora u središnjem živčanom sustavu postupno se razvija tolerancija prema nikotinu i ovisnost. Prilikom prestanka pušenja javljaju se apstinencijske teškoće uz dugotrajnu žudnju za nikotinom. Analizirali smo povezanost recidiva pušenja s rezultatima mjerenja brzine strujanja krvi (BFV) transkranijskim doplerom te stupnjem ovisnosti o nikotinu mjerene pomoću Fragestromovog upitnika. U ispitivanje je bilo uključeno 47 ispitanika (25 žena i 22 muškarca) koji su participirali u programu odvikavanja od pušenja (Breathe Free Plan to Stop Smoking) u Zagrebačkoj školi nepušenja. Nakon 12 mjeseci praćenja ispitanike smo podijelili ovisno o pušačkom statusu u tri grupe: pušači koji su kontinuirano apstinirali, pušači koji su tijekom apstinencije jedan ili više puta recidivirali, pušači koji nisu apstinirali. Ustanovili smo da su pušači s visokim stupnjem ovisnosti o nikotinu i patološkim TCD nalazom češće bili neuspješni u apstinenciji, što ukazuje na potrebu specifičnih terapijskih postupaka s više podrške i individualno prilagođenih vještina kao i promjena na kognitivnom planu, za ovu kategoriju pušača. Mjerenje brzine strujanja krvi transkranijskim doplerom kod pušača pokazalo se praktički vrijednim za predikciju recidiva pušenja.