## A. NICOTINE HAS PHYSIOLOGICAL AND CENTRAL NERVOUS SYSTEM EFFECTS

The physiological and central nervous system effects of nicotine involve effects on both the structure and the function of the brain. When it is inhaled in cigarette smoke, nicotine is absorbed into the lungs and then rapidly enters the bloodstream. In smokeless tobacco, it is absorbed through tissues of the mouth or nose and then enters the bloodstream. Once it is in the bloodstream, nicotine crosses the blood-brain barrier and is rapidly distributed to the brain.[17] It is estimated that, once inhaled in cigarette smoke, nicotine reaches the brain in 11 seconds or less.[18] Nicotine generates its effects by binding to receptors in the brain that are intended to receive the neurotransmitter acetylcholine. These receptors, when activated by nicotine, cause the release of other chemicals in the brain that produce effects on mood, alertness, and perhaps cognition. Continued nicotine use causes an increase in the number of receptors that can bind nicotine, and changes the electrical and metabolic activity of the brain.

Nicotine's rewarding effects are the result of its action on a part of the brain called the mesolimbic system, which is also affected by many other addictive drugs.[19] Nicotine, like amphetamine and cocaine, produces its rewarding or reinforcing effects by stimulating the

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[17] Surgeon General's Report. 1988. *Nicotine Addiction.* Page 13.

[18] Benowitz NL. Clinical Pharmacology of Inhaled Drugs of Abuse: Implications in Understanding Nicotine Dependence. *Research Monograph 99.* National Institute on Drug Abuse. 1990. Page 17.

[19] *See:*
Wise RA, Rompre PP. Brain dopamine and reward. *Ann Rev Psychol.* 1989;40:191-225.

Clarke PBS. Mesolimbic dopamine activation--the key to nicotine reinforcement? *The Biology of Nicotine Dependence.* Wiley, Chichester (Ciba Foundation Symposium 152) 1990;153-168.

release of dopamine, a chemical produced in the mesolimbic system. Dopamine plays a major role in regulating pleasurable sensations.[20] (See Appendix 1 for a summary of the studies indicating that nicotine acts on the mesolimbic dopaminergic system.)

Nicotine produces a range of other complex pharmacological effects that are related to its dose and/or bioavailability. For example, at low doses, nicotine stimulates the cardiovascular system, producing an increase in blood pressure and heart rate. At higher doses or more rapid administration, nicotine slows the heart rate.[21]

Depending on the circumstances, nicotine delivered by cigarette smoking can have an arousal-increasing or arousal-reducing effect.[22] These effects have been confirmed using electroencephalographic (EEG) analysis.[23] When smokers are placed in a stressful situation,

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[20] *See:*

Pomerleau OF, Pomerleau CS. Neuroregulators and the reinforcement of smoking: towards a biobehavioral explanation. *Neurosci Biobehav Rev.* 1984;8:503-513.

Wise and Rompre, note 19, *supra,* at pp. 191-225.

Clarke, note 19, *supra,* at pp. 153-168.

[21] Henningfield JE, Miyasato K, Jasinski DR. Abuse liability and pharmacodynamic characteristics of intravenous and inhaled nicotine. *J. Pharmacol Exp Ther.* 1985;234:1-12.

[22] Norton R, Brown K, Howard R. Smoking, nicotine dose and the lateralisation of electrocortical activity. *Psychopharmacology.* 1992;108:473-479.

[23] *See:*

Pritchard WS, Gilbert DG, Duke DW. Flexible effects of quantified cigarette-smoke delivery on EEG dimensional complexity. *Psychopharmacology.* 1993;113:95-102.

Pritchard WS. Electroencephalographic effects of cigarette smoking. *Psychopharmacology.* 1991;104:485-490.

Golding JF. Effects of cigarette smoking on resting EEG, visual evoked potentials and photic driving. *Pharmacology Biochemistry and Behavior.* 1988;29:23-32.

smoking can have a depressant effect on the EEG profile.[24] When smokers are under conditions of low arousal induced by mild sensory isolation, cigarette smoking can have a stimulant effect.[25] In other words, smoking appears to have a relaxing effect in stressful situations and a stimulating effect in otherwise nonstimulating circumstances.

Smoking or the administration of nicotine appears to have mixed results in its effects on sustained attention.[26] The tobacco industry has conducted several studies on nicotine's effect on performance and cognition. While some studies showed increased performance and response,[27] others showed little or no effect.[28] Many of these studies were conducted with nicotine-deprived subjects, and the results may reflect the reversal of deficiencies caused by nicotine withdrawal. The 1988 Surgeon General's Report concluded that "[a]fter smoking cigarettes or receiving nicotine, smokers perform better on some cognitive tasks . . . than they do when deprived of cigarettes or nicotine. However, smoking and nicotine do not improve general learning."[29] (An extensive discussion of the physiological and central nervous system

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[24] *See* Pritchard, note 23, *supra,* at pp. 485-490.

[25] Golding J, Mangan GL. Arousing and de-arousing effects of cigarette smoking under conditions of stress and mild sensory isolation. *Psychophysiology.* 1982;19(4):449-56.

[26] Heishman SJ, Taylor RC, Henningfield JE. Nicotine and smoking: A review of effects on human performance. *Experimental and Clinical Psychopharmacology.* 1994;2(4):345-395.

[27] *See:*
Wesnes K, Warburton DM. Effects of smoking on rapid information processing performance. *Neuropsychobiology.* 1983;9:223-229.

Wesnes K, Warburton DM. Effects of scopolamine and nicotine on human rapid information processing performance. *Psychopharmacology.* 1984;82:147-150.

[28] *See* Heishman et al, note 26, *supra.*

[29] Surgeon General's Report. 1988. *Nicotine Addiction.* Page 441.

effects of nicotine is available in the 1988 Surgeon General's Report.[30])

[30] *Id.* at pp. 381-458.