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SUNISA CHAIKLIENG : THE NEUROTOXIC EFFECTS OF ACRYLONITRILE AND NICOTINE IN RATS. THESIS ADVISORS: JUTAMAAD SATAYAVIVAD, Ph.D., NOPPAMARS WONGWITDECHA, Ph.D., SARA ARPHORN, Dr.Biol.Hum. 184 p. ISBN 974-664-691-5

The effects of subchronic exposure to acrylonitrile (ACN) and nicotine (NIC) on central cholinergic functions in male Wistar rats have been studied. Daily subcutaneous administration of NIC 0.1 (low dose) and 0.75 mg/kg BW (high dose), 5 days/week for a period of 4 and 8 weeks induced significant increases in motor behavioural activities compared to the control group receiving normal saline. It was clearly observed that the stimulating effects of high dose of nicotine were less than low dose. These alterations which include ambulatory activities, stereotypic activities, and rotational behaviours were dose- and time- dependent as recorded using an open-field test. Typical motor activities such as ataxia and straub tail were observed in high dose of nicotine-treated group. Tolerance to depressant effect of high dose and sensitization to stimulating effects of low dose on motor behavioural activities were detected after repeated exposure to nicotine. In addition, weight gain was observed following termination of nicotine administration.

ACN is a cholinomimetic chemical responsible for the decreased motor activity similar to acute effect of physostigmine. In 7 days-ACN 25 mg/kg BW, s.c. pretreated rats, following the challenge with NIC 0.1 and 0.75 mg/kg BW, s.c., ACN produced additive effects with nicotine on the ambulatory activities, stereotypic activities and rotational behaviours. The hypersensitivity of motor behavioural activities to atropine 10 mg/kg BW, i.m. was revealed in subchronic ACN 25 mg/kg BW, s.c.-treated rats for 8 weeks.

ACN (1 mg/kg BW, s.c.), physostigmine (0.5 mg/kg BW, i.m.) and atropine (10 mg/kg BW, i.m.) were used to detect the minor alterations of central cholinergic function in subchronic nicotine-treated rats. Subchronic treatment with low dose of NIC (NIC 0.1) did not alter the effects of ACN and physostigmine on motor activities. On the other hand, subchronic exposure to a higher dose of NIC (NIC 0.75) exhibited marked increases in motor activities after being challenged with ACN and physostigmine, while those of atropine were not significantly altered by both low and high doses of subchronic nicotine treatment.

The results from this study indicate certain alterations in central cholinergic function involving motor behavioural activities in rats after prolonged exposure to acrylonitrile and nicotine. The alterations of cholinergic functions in nicotine-treated rats seemed to relate more with nicotinic rather than muscarinic receptors. Moreover, this motor activity test could be used as a model to detect the subtle changes of central nicotinic and muscarinic receptors during chronic exposure to cholinotoxic chemicals.