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WACHARIN ONLA-IAD: DISTRIBUTION OF MONOAMINE OXIDASE ENZYMES IN THE BRAINS OF THE VICTIMS OF SUDDEN UNEXPLAINED NOCTURNAL DEATH SYNDROME. THESIS ADVISORS: NAIPHINICH KOTCHABHAKDI, Ph.D., PIYARAT GOVITRAPONG, Ph.D., SUCHART PHUDHICHAREONRAT, F.R.C.P.C., M.D., SOMPORN TRIAMCHAISRI, Ph.D., 199 P. ISBN: 974-661-707-9

Previous investigations on the putative patho-physiological mechanism of Sudden Unexplained Nocturnal Death Syndrome (SUNDS) known as "Lai Tai" in local northeastern Thai dialect, have consistently indicated that the cause of death in SUNDS may involve a genetic predisposing factor related to the deletion or mutation of the gene for the monoamine oxidase A (MAO-A) which is located on the human X-chromosome. The objective of the present investigation is to study the distribution and localization of MAO enzymes in the brainstems of the victims of SUNDS as compared to that in normal adult Thai males. Four autopsy verified SUNDS brains from Thai northeastern males aged between 20 and 55 years old who died with symptoms, were obtained from the autopsy room of Ramathibodi Hospital. In addition, other four normal brains were obtained from adult Thai males who died from severe injuries or other diseases which did not appear to affect the brain. Serial cryostat cross sections of the brainstems were incubated with monoclonal antibodies specifically against MAO-A, MAO-B, and MAO-AB, and the presence of the MAO enzymes was demonstrated by the Horseradish Peroxidase (HRP) reaction products in neurons which were also counter stained with Nissl's stain to allow identification and localization of various specific neuronal groups. Immuno-positive HRP labeled neurons were consistently found in brainstem sections of all four SUNDS brains after incubation with specific monoclonal antibodies against MAO-A, MAO-B and MAO-AB. The distribution and localization of these labeled brainstem neurons from SUNDS victims were remarkably similar to those found in the normal adult Thai males. On the contrary, the density of neurons in the substantia nigra (SN), and the total count of neurons in the locus ceruleus (LC), the sub-ceruleus nucleus (SC), the mid-line dorsal raphe (DR) nucleus, and the medullary (M) neurons from the brainstems of SUNDS victims were statistically significantly ($p < 0.01$) lower than those in the corresponding areas of the normal adult Thai males. The finding clearly indicates that both MAO-A and MAO-B enzymes are expressed in all SUNDS brains obtained for the present study. It is quite possible that the monoclonal antibody against MAO-A used in the present study may not be specific toward the site of the mutation on the enzyme molecule. However, the significant reduction of the density or the total population of MAO labeled neurons in many areas of the brainstem which regulate vital functions such as sleep-arousal, cardiovascular and pulmonary functions, in SUNDS as compared to the normal brains suggest that the lower amount of MAO in SUNDS brains may be an important disposing factor during certain critical states of sleep which are related to high levels of biogenic monoamines in the brainstem beyond the catalytic capability of the well-known alternating pathway utilizing Catecho-O-Methyl-Transferase (COMT) enzyme. Further definitive supporting evidence for this hypothesis in the future may come from direct assays of MAO enzymatic activities and levels of monoamines in the brains of SUNDS victims as compared to normal brains.