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TITLE : FIBER-TYPE SPECIFIC CAFFEINE SENSITIVITIES IN NORMAL AND MALIGNANT HYPERTHERMIA HUMAN SKINNED MUSCLE FIBERS

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Muscle fiber type influences the results of the caffeine contracture test in normal human skinned muscle fibers (1). It was thus of interest to investigate the difference in caffeine sensitivity in malignant hyperthermia (MH) human type I and II muscle fibers.

Caffeine sensitivity was studied in chemically skinned muscle fibers from 5 MH susceptible (MNS) and 8 normal patients (MHN) with informed consent and approval by the research committee (Univ. Lille). Muscle fiber type was determined by contracture occurring in strontium (type I fiber) or calcium (both type I and type II fiber) solutions and in 15 fibers after contracture testing by ATPase enzyme histochemistry. Caffeine sensitivity was defined as the threshold concentration inducing more than 10 % of the tension developed by 40 mM caffeine. Statistical analysis was performed using Student's t test for mean comparisons.

In normal muscle, type I fibers had higher sensitivity than type II fibers (P<0.05) whereas an increase in caffeine sensitivity was found in both type I and type II fiber from MHS patients. The mean caffeine threshold of type I MHS fibers was not statistically different from those of type II MH fibers (table 1). The findings that both type I and II MH fibers had higher caffeine sensitivity than normal fibers greatly strengthened the validity of the in vitro contracture test done in muscle strips containing type I and type II fibers in varying proportions (2).

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- 1) Anesthesiology 72 : 50-54, 1990
2) Anest. Analg. 69 : 437-443, 1989

Caffeine sensitivity (mM)

Fiber type	MHS	MHN
I + II	2.71±1.78(49)	9.14±3.90(61)*
I	2.29±1.65(27)	6.26±2.04(23)*
II	3.22±2.32(22)	10.89±3.73(38)**

Table 1 : Fiber type specific caffeine threshold concentration in MH susceptible (MHS) and MH non susceptible patients (MHN). Values are means±SD. Number of fibers tested given in parentheses.

* p<0.05 as compared to the corresponding values in MHS fibers. + p<0.05 as compared to MHN type I fiber.

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TITLE : THE CALCIUM AGONIST BAY K 8644 POTENTIATES THE ISOFLURANE/HALOTHANE IN VITRO CONTRACTURE RESPONSE OF MALIGNANT HYPERTHERMIA SUSCEPTIBLE MUSCLE TO THE SAME EXTENT

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Malignant hyperthermia (MH) can be triggered by both genetic factors and environmental conditions. Genetic factors are easily determined on the basis of the in vitro halothane and caffeine (HC) test results (1). In contrast, isoflurane (I) has a lesser ability to induce contracture in MH muscle in vitro (2). This does not necessarily mean that I is less lethal trigger of MH than H in vivo (3). A hypothesis was tested that an up modulation of the dihydropyridine receptor (DHPR) of the T-tubules by a Ca++ agonist BAY K 8644 may mimic one of the environmental conditions that triggers I-induced contracture in vivo.

Fourteen MH susceptible patients (MHS) and 14 MH non susceptible (MHN) patients were investigated with informed consent and approval by the Research Committee (Univ. of Lille). In addition to the usual HC tests (1), other muscle strips were exposed to BAY K + H and equipotent anesthetic concentrations of I alone and BAY K + I. I-induced contractures in MHS muscles was less than H (p<0.05). BAY K did not induce contracture on its own but considerably enhanced both the H and I effects to the same extent. Such effect was not observed in the MHN group.

These results clearly show that the up modulation of the DHPR by a calcium agonist can mimic the environmental conditions leading to I to be as potent MH trigger as H.

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- 1) Br J Anaesth 56 : 1267-1270 2) Can Anaesth Soc J 27 : 12-15, 1980 3) Br J Anaesth 59 : 1196-1198, 1987

MHS HAC	H alone n=14	H +BAY K n=10	I alone n=14	I +BAY K n=10
0.5	0.18(0.22)	1.03(0.39)+	0.06(0.11)*	1.00(0.41)*
1.0	0.44(0.44)	1.05(0.43)+	0.15(0.16)*	0.56(0.32)*
2.0	0.65(0.36)	0.76(0.43)+	0.17(0.18)*	0.47(0.40)*
3.0	0.58(0.27)	0.67(0.34)+	0.17(0.17)*	0.35(0.34)*

MHN HAC	H alone n=14	H +BAY K n=14	I alone n=14	I +BAY K n=14
0.5	0	0.02(0.04)	0	0.02(0.08)
1.0	0	0.08(0.15)	0	0.03(0.06)
2.0	0	0.22(0.21)	0	0.02(0.06)
3.0	0	0.29(0.24)	0	0.04(0.09)

Changes in tension (g) with H, H+BAY K, I, I+BAYK in MHS and MHN muscle strips (n) ; values are means ± SD ; statistical analysis using Student's paired t-test+and* p<0.05 compared with H alone *p<0.05 compared with H and I alone.