Introduction: Malignant hyperthermia (MH) is considered to be an inherited disease of muscular metabolism. Some findings indicate however that other organs may also be primarily affected in the development of MH. Despite the observation that outcome in MH survivors is often determined by neurological complications encountered during an MH episode only few studies have been done on the effect of central nervous structures during MH (1,2). This study evaluates the electroencephalographic changes in the development of MH in swine in correspondence to the well-known hemodynamic and blood gas analytical findings.

Methods: 10 malignant hyperthermia susceptible (MHS) (Pietrain: 22-38 kg, age: 3-5 months) and 10 not MH-susceptible (nMHS) pigs (Yorkshire: 32-48 kg, age: 4-6 months) took part in the study. After intraperitoneal premedication with azaperon (Stresnil®; 30-50 mg) and xylazine (Rompun®; 0.5 ml) induction of anesthesia was achieved with methohexitol (100-150 mg i.v.). After pharyngeal intubation of lignocaine 4% endotracheal intubation was performed following manual hyperventilation with 100% oxygen. Anesthesia was achieved by methohexitol 20-40 mg/kg and nitrous oxide in oxygen (FiO2=0.5; 6 l/min). Ventilation was set for endexpiratory carbon dioxide tensions (PetCO2) of 34-38 mmHg (Capnograph®). The femoral artery and veins were cannulated for blood pressure (AP) and central venous pressure (CVP) monitoring. Cardiac output (CO) was measured after injection of 5 ml cold (5-10°C) saline solution by thermodilution via a pulmonary catheter (5F, Cardiosept E-4®) placed in a "wedge"-position. For each single point 3 succeeding CO-measurements were averaged and cardiac index (CI) calculated as 1/l0kg/min. The following hemodynamic parameters were stored on magnetic tape (Store 7DS®): ECG, AP, PetCO2: Body temperature was measured with rectal and deep esophageal thermistors. Needle electrodes for electroencephalographic recordings (EEG) were placed at a position corresponding to vertex in humans (Cz) with linked earlobes (A1-A2) as a reference and at parietal sites (corresponding to C3 and C4 in man) with a frontal reference (Fz). The electro-oculogram (EOG) was recorded from supra- vs. infraorbital electrodes. Bandpass was set at 0.5-30 Hz. After amplification the analog signals were stored on magnetic tape. The power spectra were analyzed after Fourier transformation (FFT, epoch length: 5.2 sec, 100/sec). All data were grouped into time intervals of 5-10 min length for the period after admixture of halothane (1%). Data between time periods in MHS- and nMHS-animals were subjected to analysis of variance (ANOVA) and where statistical significance could be assumed (p<0.05) Duncan's procedure for repeated measurements was performed. Data of MHS vs. nMHS-animals were subjected to paired t-test (p<0.05).

Results: Simultaneously to an increase of PetCO2 in MHS-animals 30-40 min after the beginning of halothane admixture a decrease in total EEG-power could be noted, whereas in control animals no such changes occurred (Fig. 1). At this time in the MHS-group heart rate (HR) (127±35/min), AP (76±25 mmHg) and CI (12±0.31 l/10kg/min) indicated a hyperdynamic circulatory response. Other findings at the time of onset of EEG-changes were: arterial oxygen tension (PaO2): 102±25.2 vs. 111.5±23.3 (baseline); arterial CO2: 49.2±5.1 vs. 35.6±3.8; central venous oxygen tensions (PVCO2: 45.1±13.9 vs. 51.9±10.1); arterial pH: 7.35±0.12 vs. 7.40±0.13; arterial plasma levels K+: 5.31±0.65 vs. 4.99±0.61; Na+: 145±1.31 vs. 142.8±2.2. Body temperature was not different from baseline values. EEG-power steadily decreased during the following time periods until a flat EEG was recorded in 6 animals. Simultaneously a shift in frequency to lower frequencies occurred. Only in 2 animals spike-wave-complexes could be noted.

Discussion: For successful treatment of MH early diagnosis is of utmost importance. Whereas our data cannot prove a primary role of CNS during MH it was clearly demonstrated that EEG changes do occur very early in the development of MH. These EEG alterations (shift in frequencies, decrease in total power) cannot only be explained by an increase in PaCO2 respectively a decrease in PaO2 or pH as the values of these parameters were still within their physiologic ranges, when the first EEG-responses were noted. In MHS-swine body temperature rose with a time-lag of 3-20 min to PetCO2 and EEG-changes.

References:
1. Artru AA, Gronert GA; Cerebral Metabolism during Porcine Malignant Hyperthermia. Anesthesiology 53:121-126, 1980