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# The DC-Recorded Dog Electroretinogram in Ketamine – Medetomidine Anaesthesia

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**Kommonen, B: The DC-recorded dog electroretinogram in Ketamine – medetomidine anaesthesia. Acta vet. scand. 1988, 29, 35-41.** – A new selective alpha 2-adrenoreceptor agonist, medetomidine hydrochloride was combined with low dosage ketamine hydrochloride and vecuronium bromide for d.c. (direct current) recordings of fast electroretinographic (ERG) components in nine ophthalmoscopically healthy dark adapted dogs. The dogs were tracheally intubated and manually ventilated. They were given full field single flash stimuli of different intensities starting with near b-wave threshold blue light (tests 1-3), followed by white light (tests 4-6) and 30 Hz photopic flicker (test 7). The a- and b-wave amplitudes and flicker responses were measured from the base line. The latencies were measured from the stimulus moment to the highest point of the different waves.

Statistical analysis of results gave individual differencies which had a good constancy. This showed that the dogs had an individual ERG profile according to the standardized method. The latencies varied very little as expected, but the amplitudes differed individually and showed a good constancy as seen by reproducibility tests made nine to ten days later on three of the dogs' ipsilateral eyes. The combination of drugs used in this study was considered suitable for short term (10-12 minutes) stable d.c. – ERG recordings in dogs as the rod and cone responses had higher amplitudes when compared to an identical examination made with other anaesthetic combinations on the same dogs.

Involuntary eye movements and other involuntary muscular activity caused by ketamine in dogs were negligible when using medetomidine premedication and was completely absent when using vecuronium.

The anaesthetic method described can be recommended for ambulatory ERG recordings in dogs because of the above mentioned advantages.

electrophysiology; retina; canine.

## Introduction

The amplitudes of the different electroretinographic (ERG) components are usually depressed by anaesthetics (*Knave et al.* 1974, *Raitta et al.* 1979, *Brown & Green* 1984, *Jarkman et al.* 1985, *Tashiro et al.* 1986). The depressant effect of the anaesthetics can mask subtle changes in the a-, b-and c-wave amplitudes of the ERG when studying retinal responses to low intensity stimuli, and especially when early stage retinal dystrophies are studied under such conditions.

In a recently made study (*Kommonen et al.* 1988) the effect of 2 different anaesthetic methods on the ERG rod and cone response was investigated using ophthalmoscopically healthy dogs. One of the anaesthesias studied was ketamine combined with xylazine.

That combination of anaesthesia proved to be superior to a combination of thiopentone, halothane and nitrous oxide in oxygen because of less depressing effects on especially the receptor response. Additionally, ketamine alone combined with a non-depolarizing neuromuscular blocking agent was tested on 3 dogs. This gave even better responses than when using ketamine combined with xylazine. Ketamine as a sole agent in dogs, however, has unwanted side effects such as occasional nystagamus and muscular twitching and often leading to a cateleptoid state in dogs (*Benson et al.* 1985, *Haskins et al.* 1985, 1986). Therefore it was important to search for an anaesthetic method that interferes with the production of the retinal action potentials as little as possible, but still would give a base line as free of eye movement caused artifacts as possible and that would result in an eye globe that is straight without suturing.

The use of a suitable premedication to ketamine allowed the ketamine dose to be considerably lowered (from 10 to 1.5 mg/kg).

The purpose of this study was to find out if the combination of an intramuscular dosage of medetomidine hydrochloride with a low intravenous dosage of ketamine hydrochloride followed by a short acting non depolarizing neuromuscular blocking agent, vecuronium bromide, it a good choise for clinical electroretinographic recordings in the dog.

## Material and methods

Nine ophthalmoscopically healthy dogs were examined. Characteristics of the dogs are presented in Table 1. All dogs and eyes were identical with the ones used in the earlier study (*Kommonen et al.* 1988). Two 8 year old Beagles, used in the earlier work were excluded. The dogs were premedicated with glycopyrrolate 0.01 mg/kg (Gastrodyn$^R$ 0.2 mg/ml, Medica, Finland) and medetomidine hydrochloride 15 µg/kg intramuscularly (aqueous solution 1 mg/ml, obtained from Farmos Research Center, Turku, Finland). Medetomidine hydrochloride ( (±)-4 (α, 2, 3, - trimethylbenzyl) -imidazole hydrochloride is a rather selective alpha 2-adrenoreceptor agonist (*Savola et al.* 1986). Both drugs were given immediately after each other and simultaneously with the mydriatics tropicamide and cyclopentolate hydrochloride (two drops of each) (Oftan Tropicamid$^R$ 5 mg/ml and Oftan Syklo$^R$ 5 mg/ml, Star, Finland). Twenty min. after the premedication 1.5 mg/kg ketamine hydrochloride (Ketalar$^R$ 10 mg/ml, Parke Davis, UK) was injected intravenously and the dogs were pre oxygenated. This was followed by an intravenous administration of vecuroniuim bromide 0.2 mg/kg (Norcuron$^R$ 4 mg/ml, Organon, Holland). After administration of the neuromuscular blocking agent, ventilation was manually controlled with oxygen using a conical face mask. Shortly thereafter the dogs were tracheally intubated and manually ventilated with an air/oxygen mixture using a non re-breathing system with a Ruben valve. After premedication, after ketamine, before ERG recordings (after vecuronium) and after recordings electrocardiography (ECG) was performed on all of the dogs (Cardiovit CS-6 electrocardiograph, Schiller, AG, Ch-6340 Baar, Switzerland). During ERG recordings ECG and $CO_2$ measurements were not performed because of disturbances in the ERG. Exhaled end-tidal $PCO_2$ was monito-

Table 1. Characteristics of the dogs used in the study.

| Number of dogs | Breed (years) | Age (kgs) | Weight | Eye |
|---|---|---|---|---|
| 7 | Beagle | 1½-2 | 9-12.5 | 7 Left |
| 2 | Beagle/ Finnish harrier | 3¼ | 12-14 | 2 Right |

red by a $CO_2$ analyzer ($CO_2$ analyzer D 300, Datex, Instrumentarium, Finland). After the recordings the neuromuscular blockade was reversed by metastigmine with atropine. Reproducibility tests of the ERG recordings was performed 9-10 days later on 3 of the dogs using identical anaesthesia and identical stimulating and recording techniques.

The stimulating apparatus, electrodes and recording apparatus and a detailed description of the electrophysiologic examination has been published (*Kommonen et al.* 1988). The dogs were kept in dimly lighted dog cages for at least 1 h before the examination. The dark adaptation was started immediately after application of the premedication and mydriatics. The dark adaptation time ranged from 30 to 47 min (mean 36 min). Oxybuprocaine hydrochloride eyedrops (Oftan Obucain$^R$ 4 mg/ml, Star, Finland) were instilled in the eye. In all anaesthesias the stimulus intensities and sequence were identical to those described earlier (*Kommonen et al.* 1988). Six single flashes of different intensity were delivered at 1½ min intervals. As a seventh Test a 30 Hz photopic flicker stimulus was delivered after light adaptation. The filters used and the relative intensities of the test flashes, referred to as tests 1-7, are shown in Table 2.

Table 2. Intensity of the different test flashes.

| Test Flash N:o | Filters used | Log relative units above Test 1 |
|---|---|---|
| 1 | ND 1, ND 2, KW 47 B (blue) | 0 |
| 2 | ND 1, KW 47 B | 2 |
| 3 | ND 0.6 KW 47 B | 2.4 |
| 4 | ND 2 | 1.7 |
| 5 | ND 1 | 2.7 |
| 6 | - | 3.7 |
| 7 | - | 2.3 |

*Statistical methods*

Median was used as a nonparametric statistic for central tendency and quartile deviation (d) for dispersion and still the range interval was used for description of the observations.

In order to get some comprehension on the consistency of observations the intra individual correlation of 3 replicates was calculaed. The estimates of variances for observations of 9 dogs ($S_b^2$) were calculated as well as estimates on the basis of the differences in replicates ($S_w^2$). The coefficient of the intra individual correlation Rw was estimated on the basis of the equation:

$$R_w^2 = \frac{S_b^2 - S_w^2}{S_b^2}$$

$S_b^2$ = variance between all observations

$S_w^2$ = variance of the observations in the same individual

This coefficient was calculated only for amplitudes because of the small variation in latencies.

## Results

*Electroretinography*

The amplitudes and latencies of a- and b-waves under different intensities, referred to as test 1-6, and 30 Hz photopic flicker stimuli (Test 7) are seen in Table 3 and 4 respectively.

The level of $R_w$:s was mainly high. The median for a-waves was 0.89 and 0.92 for b waves. This meant that the observations on the dogs, which represented a rather homogenous group, gave individual differencies which had a good constancy. ERG recordings from one of the beagle bitches is seen in Fig. 1.

The repeatability of some observations, shown for Test 2 (low intensity blue light, mainly rod and rod mediated response) and for Test 7 (30 Hz photopic flicker response, cone mediated response), can be seen in Ta-

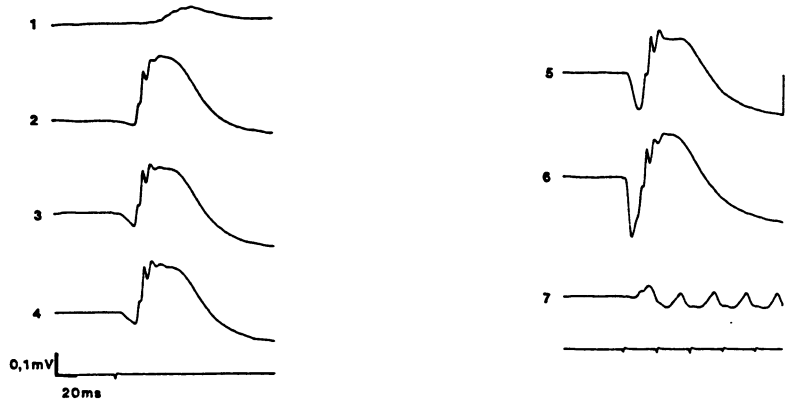


Figure 1. ERG recordings from one of the Beagles. Test 1 shows a typical response to the lowest intensity used. The positive deflection (after convention upwards = positive) after stimulation is called the b-wave, which originats mainly from the bipolars. The a-wave, which has its origin in the receptors in still missing at this intensity. In the second recording (Test 2) a small negative deflection, the a-wave originating from the receptors is seen directly after the stimulus. The stimulus moment is indicated under the recordings as a small deflection on the line with time and amplitude calibration. The first deflection on the line under the flicker response (Test 7) also indicates the stimulus moments of Tests 5 and 6. The significance of a disturbance free base line as seen in the recordings is obvious for evaluation of the a-wave amplitude at low intensities as in test 2.
Tests 3 and 4 show practically identical responses in spite of different intensities and different spectral distribution of the test flashes. A relative lowering of the b-wave in relation to the a-wave is seen already after Test 2. Shortening of especially the a-wave latencies is seen at higher intensities (Tests 5 and 6). Oscillatory potentials are superimposed on the b-waves of tests 1-6.
Test 7 shows a typical 30 Hz photopic flicker response.

Table 3. Amplitudes and latencies of a-waves under different intensities.

| | Amplitudes (μv) | | | | Latencies (ms) | | |
|---|---|---|---|---|---|---|---|
| Test No | Range | Median | d | Rw | Range | Median | d |
| 1 | -* | - | - | | - | - | - |
| 2 | 14-38 | 35 | 5.3 | 0.81 | 18-22 | 20 | 1 |
| 3 | 45.5-115 | 91 | 21.9 | 0.96 | 17-20 | 19 | 0.75 |
| 4 | 42-126 | 87.5 | 21.8 | 0.77 | 17-20 | 19 | 0.75 |
| 5 | 105-308 | 178 | 50 | 0.90 | 13-17 | 15 | 2 |
| 6 | 192-430 | 329 | 51.8 | 0.89 | 7-8 | 8 | 0.4 |

* The a-wave was not recordable using this intensity.

ble 5. The results of a repeated examination made 9-10 days later on the same eye of the same dogs are in parenthesis. The repeatability described in these examples was similar in the main features for the other Tests (1, 3, 4, 5 and 6).

*Anaesthesia*

The dogs showed light grade sedation and reduced muscular tone already a few minutes after the administration of the premedication. Duration of the ERG examination was 10-12 min. The induction doses of the

Table 4. Amplitudes and latencies of b-waves under different intensities.

| | Amplitudes (μv) | | | | Latencies (ms) | | |
|---|---|---|---|---|---|---|---|
| Test No | Range | Median | d | Rw | Range | Median | d |
| 1 | 7–147 | 77 | 38.4 | 0.84 | 67–77 | 72 | 2 |
| 2 | 164–469 | 273 | 69 | 0.93 | 39–53 | 43 | 2.2 |
| 3 | 98–420 | 189 | 56 | 0.92 | 31–42 | 33 | 1.5 |
| 4 | 105–588 | 217 | 61.2 | 0.77 | 31–42 | 33 | 1.8 |
| 5 | 45.5–413 | 126 | 97 | 0.95 | 29–33 | 33 | 1.2 |
| 6 | 3.5–364 | 94 | 99 | 0.98 | 27–40 | 30 | 3.2 |
| 7 | 35–90 | 70 | 15 | 0.80 | 21–24 | 22 | 0.25 |

anaesthetics provided sufficient anaesthesia for this examination. All dogs recovered uneventfully from the anaesthesia. End tidal $CO_2$ concentration was $< 5\%$ in all dogs during anaesthesia (generally 4-5%).

The heart rate increased after the administration of the premedication, and it did not quite reach base line values when recorded immediately after the ERG. In one dog the QRS (heart ventricular) complex after the P wave was occasionally missing.

The eye globes of the dogs were in 6 cases straight, but 3 eyes showed a slight tendency to ventronasal rotation. The slight ventronasal rotation diminished after ketamine and dissappeared completely after the administration of vecuronium. The pupils were maximally dilated and no light response could be observed when checked immediately after the recordings. No corneal irritation was observed after the examination. Cyclopentolate caused light grade conjunctival irritation in the dogs.

Table 5. The a- and b-wave amplitudes and latencies of test 2 and corresponding values of b-waves in test 7 of the first and repeated examinations (in parenthesis) of 3 of the Beagle dogs

| | Test 2 (low intensity blue light) | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | a-wave | | | | b-wave | | | |
| Dog ear nr. | ampl. in μV | | lat. in ms | | ampl. in μV | | lat. in ms | |
| 035G | 17.5 | (17.5) | 22 | (20) | 220 | (266) | 43 | (45) |
| 061E | 35 | (45.5) | 20 | (20) | 469 | (525) | 43 | (43) |
| 07G | 35 | (28) | 18 | (20) | 301 | (350) | 39 | (47) |

| | Test 7 (30 Hz photopic flicker, white light) | | | |
|---|---|---|---|---|
| Dog ear nr. | ampl. in μV | | lat. in ms | |
| 035G | 60 | (65) | 21 | (21) |
| 061E | 90 | (100) | 22 | (22) |
| 07G | 50 | (65) | 22 | (22) |

## Discussion

As stable, reliable, single flash ERG recordings from dogs have to be performed in anaesthesia or deep sedation, anaesthetics interfering as little as possible with the retinal action potentials must be considered superior to those which affect the latter to a higher degree. The combination of medetomidine with ketamine in the described dosage resulted in an analgetic and anaesthetic state that allowed the use of an ultra short acting neuromuscular blocking agent followed by subsequent tracheal intubation. It has to be pointed out that intravenous ketamine at this dosage resulted in a short anaesthesia, which proved sufficient for the recordings made in this study. The use of the neuromuscular blockade was advantageous because of the lack of muscular activity that usually results in more or less great irregularities on the base line. The method resulted in a practically disturbance and drift free base line even at long registration times of 10 s which are needed for registration of the c-wave.

As good single flash ERG recordings from dogs cannot be made in a state completely free from pharmacologic influence, the physiological dog ERG is impossible to achieve. The anaesthetic method described had the least depressing effect on the amplitudes of all the anaesthetic and sedative methods tested by the author and his collaborators for dog ERG recordings. A study using the same stimulating and recording method was undertaken using other combinations of anaesthetics and sole anaesthetics in the same individual dogs, using the same eyes (*Kommonen et al.* 1988).

The exact mode of action of the drugs used in this study can only be speculated upon. It seems that a combination of medetomidine, ketamine and vecuronium would interfere very little with the hyperpolarization of the receptors themselves after photic stimulation (high a-wave). This assumption is based on the hypothesis that dogs would show still higher receptor responses (a-wave) in the unanaesthetized state. This has been shown for ketamine in rabbits (*Sasovets* 1978).

Because individual dogs have quite large differences in a- and b-wave amplitudes the neccesity to test the reproducibility of recordings is obvious. The method used showed good reproducibility of observations. The small difference in results of the reproduced examinations when compared to the first examination can be caused by intrinsic or extrinsic factors. Intrinsic factors could have their origin in the retinal metabolism. Extrinsic factors could be based on the slight differencies in position of the eye in the full field illuminator, or in the conductance of the electrodes, or slightly differing light history before starting the dark adaptation.

Test 1 b-wave represents a rod mediated response and test 2 a-wave mainly a rod response. Test 7 oscillations represent cone mediated responses (*Aguirre* 1975). In this investigation the dogs had an individual ERG profile which was very little influenced by the method of examination. The well standardized method using quantitative anaesthesia can be recommended for short term ERG recordings in dogs.

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**Sammandrag**

*Likströms förstärkt registrering av elektroretinogram på hund i ketamin - medetomidin anestesi.*

En ny selektiv alfa 2-adrenoreceptor agonist, medetomidin hydroklorid kombinerades med en låg dos ketamin hydroklorid och vecuronium bromid för registrering av likströmsförstärkt elektroretinografi (ERG) på 9 oftalmoskopiskt friska mörkeradapterade hundar. Hundarna intuberades och ventilerades manuellt. De gavs enskilda blixtar av olika intensitet över hela synfältet börjande med blått ljus nära b-vågens retningströskel (test 1-3) följda av vitt ljus (test 4-6) och 30 Hz fotopiskt flimmer (test 7). Amplituderna av a- och b-vågorna och flimmer responserna mättes från noll-linjen. Latenstiderna mättas från stimulustidpunkten till den högsta punkten på de enskilda vågorna. Statistisk analys av resultaten påvisade individuella skillnader med god konstans. Hundarna hade en individuell ERG profil enligt den standardiserade metoden. Latenstiderna varierade mycket litet, men amplituderna varierade individuellt och visade sig ha god konstant enligt resultaten av en reproducerbarhets undersökning som gjordes 9-10 dagar senare på samma ögon på 3 av hundarna. Kombinationen av de använda preparaten ansågs vara lämplig för kort (10-12 min), stabil likströmsförstärkt ERG på hund emedan stav och tapp responserna hade högre amplituder än under andra kombinationer av anestetika undersökta på samma hundar.

Ofrivilliga ögonrörelser och muskelryckningar förorsakade av ketamin hos hund minskade betydligt med medetomidin premedikation och dylika fenomen försvann helt efter applicering av vecuronium. Den beskrivna anaestesimetoden kan rekommenderas för ambulatorisk ERG på hund på grund av de beskrivna fördelarna.

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