Non-invasive Blood Pressure Monitoring in the Cynomolgus Monkey (Macaca fascicularis): High-Definition Oscillometry versus Implanted Telemetric Devices

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Introduction

The availability of accurate, repeatable and quick time response measurements is necessary for an arterial blood pressure monitoring system (Valero et al. 2006). Currently, approaches for accurate blood pressure determination rely predominantly on invasive techniques. However, chronic toxicologic studies in cynomolgus monkeys require non-invasive methods that should meet all stated necessities and are applicable for a large number of animals and day-by-day routines. The present work evaluates the high-definition oscillometry (HDO) technique as a potential non-invasive approach for accurate blood pressure recordings in cynomolgus monkeys. HDO yields stable, real-time control of each measurement on a screen by the use of blood pressure amplitude scans with up to 16,000 Hz within 10-15 sec (Figures 1 and 2).

Animals, Material and Methods

Eighteen adult cynomolgus monkeys (12 males, 6 females) were used in the study. Mean body weight was 3.9 kg (male) and 3.8 kg (female). Six male cynomolgus monkeys chronically implanted with telemetry transmitters were used for simultaneous telemetric and HDO measurements. HDO was performed by Memo Diagnostic (MDI) 1:90:90 (S+B medVet GmbH, Babenhausen, Germany).

Monitoring in Conscious Animals

The animal was restrained in a prone position with the blood pressure cuff fixed on the animal’s right upper arm. After an adaptation period, the measurements were started and resulted in values for systolic (SYS), diastolic (DIA), mean arterial blood pressure (MAP) and pulse rate per min. In conscious, non-restrained animals, these parameters were determined 15 times for each animal in one session and resulted in an average value for each individual for each parameter in the two following days, this procedure was repeated.

Monitoring During Anesthesia

All females were measured by HDO every minute under two anesthetic regimens: Ketamine (10 mg/kg BW) and Ketamine-xylazine (Ketamine 10 mg/kg BW, Xylazine 0.25-0.3 mg/kg BW). Statistical analyses were performed by the use of SigmaPlot 9.0 (SPSS Inc., Chicago, IL, USA) and a P value of < 0.05 was considered significant.

Results

When MAP was determined the first time, the HDO measurements detected significant differences between males and females due to a significantly elevated BP in males being first-time restrained (P<0.05). Such a significant sex difference disappeared in the consecutive days of measurement and resulted in an average MAP of 95 mm Hg for males and 87 mm Hg for females at day 3.

Both telemetry and HDO revealed a nearly twofold decrease of heart rate under Ketamine-xylazine anesthesia (Figure 6). Data for pulse rate were comparable whereas data for MAP were consistently higher and more variable in telemeterized animals when compared to HDO measurements (Figure 5). Twenty five ± 2 minutes after dosing, a comparable tight standard deviation like in direct techniques. The elevated MAP in first-time restrained animals might be traced back to the excitement of the adult and fully mature males not yet used to the procedure. Same as implanted telemetry, HDO is able to detect drug-related cardiovascular changes. The limited variation in our study reflects the high reproducibility, feasibility and accuracy of blood pressure measurement in M. fascicularis by HDO even in conscious animals.

Discussion

As gold standard for blood pressure measurement, direct invasive techniques are seen although they have variable degrees of invasively (Valero et al. 2006). Literature review for blood pressure values in macaques (Table 2) may lead to the same assumption since standard deviations in direct measurements are very narrow in regard to oscillometry. However, our own results gained by non-invasive HDO (Table 1) show a comparable tight standard deviation like in direct techniques. The elevated MAP in first-time restrained animals might be traced back to the excitement of the adult and fully mature males not yet used to the procedure. Same as implanted telemetry, HDO is able to detect drug-related cardiovascular changes. The limited variation in our study reflects the high reproducibility, feasibility and accuracy of blood pressure measurement in M. fascicularis by HDO even in conscious animals.

Table 1. MAP in M. fascicularis – Own Results, Differentiated by Method

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Table 2. MAP in Macaques – Literary Review

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Conclusions

HDO provides the ability and accuracy to detect drug-related cardiovascular changes non-invasively.

HDO generates data that correspond to those gained by invasive techniques and are applicable for large number of animals and day-by-day routines.

HDO may be regarded as an alternative for invasive surgeries in macaques used as an animal model for cardiovascular research.

Literature


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Presented at the 47th Annual Society of Toxicology Meeting and ToxExpo™
Seattle, Washington
16–20 March 2008