The compact integrated pupillograph CIP® (AMTech)- its value on detection of psychophysical disorder caused by drugs

Priemer, F.; Sachs, H.

Institute of Legal Medicine, University of Munich, Germany
Frauenlobstrasse 7a, 80337 Munich

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Abstract
There has been a renaissance of pupillography in Germany since the beginning of the 90s, concerning several subjects of human medicine, e.g. ophthalmology, psychiatry, otolaryngology or pharmacology. Changes of pupil reaction allow an exact interpretation of brain function because of the autonomous innervation of the pupil muscles. E.g., the group around Wilhelm, Tübingen (Germany), described characteristic pupil oscillations in subjects with sleep apnea (OSAS). Considering the increase of drug influenced drivers, it becomes more and more necessary to create tests to identify drug influenced drivers. Since 1995 we have access to the compact integrated pupillograph CIP®, which allows reliable measurements of pupil dynamics as well as eye movements. The principle of measurement is based on infrared reflection.
Up to now, the following items have been examined by the CIP®:

- onset of sleepiness waves (SW) during alcohol impairment,
- onset of the horizontal-gaze-nystagmus (HGN) during alcohol impairment,
- impairment of the pupillary light reflex (PLR) during influence of alcohol or cannabis,
- saccadic eye movements (SEM) during influence of alcohol or cannabis,
- impairment of the pupillary light reflex and of saccadic eye movements during sleep deprivation.

The device seems to be very effective to examine effects of various psychoactive substances on brain function or vision control, respectively. The CIP® is a mobile measuring device, which could also be used in the field. At the present, the interpretation of results is difficult because of the missing baseline values of the same subject in a sober state. But first results of a running study with ecstasy and some examinations in front of a disco confirm the impression, that the CIP® as a pretest device for recognition of drug impaired drivers is probably not only a vision. key words: pupillography, pupillometry, saccadic eye movement, drugs, roadside-test

Introduction

Pupillary reactions have been studied for centuries. Their use in physiologic research as indicator for autonomic nervous activity began in the eighteenth century, and interest grew in the nineteenth century, e.g. Horner's description of the effects of peripheral sympathetic lesions in man [1].

There has been a renaissance of pupillography in Germany since the beginning of the 90s, concerning several subjects of human medicine, e.g. ophthalmology, psychiatry, neurology, otolaryngology or pharmacology.
In drug development light evoked pupillography is used for monitoring of autonomic effects of the drugs[2]. But also neurodegenerative lesions lead to changes in pupillary function [3]. Spontaneous oscillations of the pupil, so-called sleepiness-waves (SW), can be detected in sleep-deprived subjects or hypersommniacs by pupillography [4,5]. This method allows an evaluation of therapy in sleep disorders, e.g. sleep apnea (OSAS) [6].
Also voluntary (saccadic eye movements) and automatic eye movements (nystagmus) are changed e.g. during alcohol impairment [7,8] or various brain disorder [9].
Considering the increase of drug influenced drivers, there is a need of simple and effective tests for their identification by authorities.

Measuring Device
Since 1996 the Compact Integrated Pupillograph CIP® (AMTech, Weinheim, Germany) has been used in various experiments as a measuring device based on infrared (IR) reflection. An infrared-sensitive CCD-line camera (up to 250 frames/s) detects the reflected IR-light, emitted by two IR-diodes. The internal software calculates the left and right margin of the pupil. This information is used to measure the pupil dynamics (pupillary light reflex, spontaneous pupillary oscillation test) or eye movements (saccadic eye movement, nystagmus). A personal computer or a laptop was used for controlling the CIP respectively storing the data.

Results

- Onset of sleepiness waves during alcohol impairment

The study was performed to work out whether alcohol as a sedative drug causes sleepiness waves. 17 healthy volunteers took part in the study. The alcohol intake was 0,8-1,0 g/kg*body mass within 2 h. 11 of them drank alcohol for the next 2 h to get a steady-state of the blood-alcohol-concentration (BAC). Spontaneous pupil behaviour was continuously detected in total darkness over 11 min. SW are characteristic and slow rhythmic contractions of the pupil, which appear, if the central activity is lowered. When SW were detected, the subjects were asked to calculate in order to differentiate whether they were able to suppress the SW (+) by central activation or not (-). After 2 h the onset of SW was heterogeneous, but after 4-5 h, in the steady-state, most of them showed SW very clearly, more often non suppressible (-) [10]. This effect was reversible in the alcohol elimination period (see figs. 1-3 as an example).

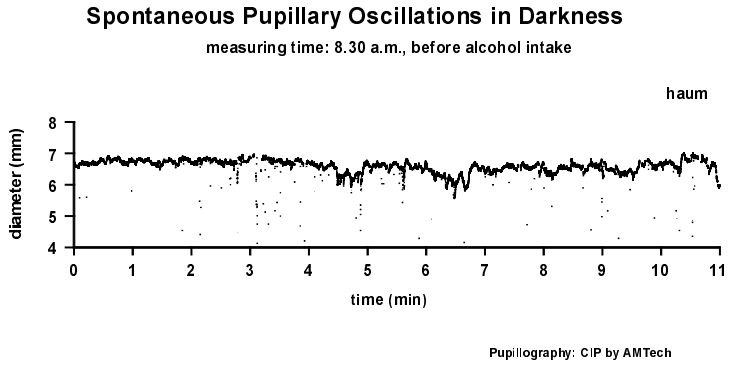

Figure 1: Pupillogram of subject 14 („haum“) before alcohol intake, mt: 8.30 a.m. No SW.

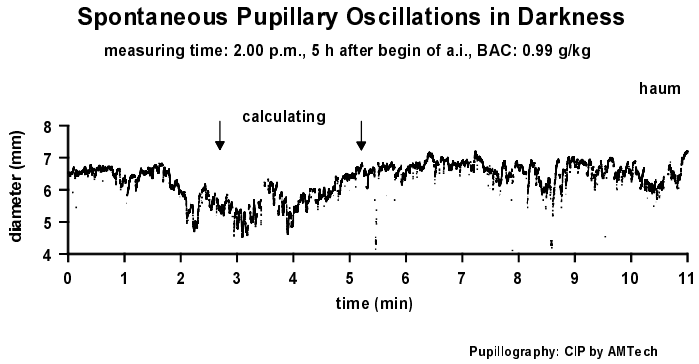

Figure 2: Pupillogram of subject 14, 5 h after beginning of a.i., mt: 2.00 p.m., BAC 0.99 g/kg. Between the arrows the subject was asked to calculate SW, non-suppressible.

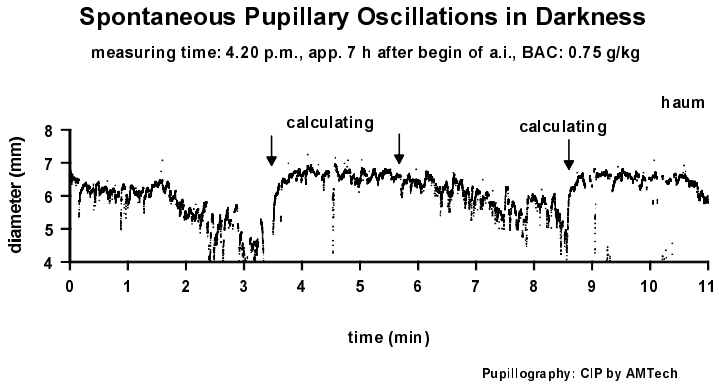

Figure 3: Pupillogram of subject 14, app. 7 h after beginning of a.i., mt: 4.20 p.m., BAC 0.75 g/kg. Between the arrows the subject was asked to calculate. SW, suppressible by calculating during the elimination period.

- Onset of the horizontal gaze nystagmus during alcohol impairment

Aim of this study was to show, if the CIP® is suitable to detect the horizontal gaze nystagmus (HGN). 15 healthy volunteers took part is this study. The alcohol load amounted between 0,99 and 1,22 g/kg*body mass within 1,5 h. Peak blood alcohol concentration levels between 0,77 and 1,34 g/kg (ppt) were reached 30-60 min later. Onset of HGN after alcohol intake was registered in all cases. In two cases, a HGN could be seen in sober state, already, but was much enhanced during alcohol load.

- The pupillary light reflex (PLR) can be measured by the CIP® in an easy way. After a 200 ms lasting light stimulus (three to four different light intensities) the pupillary constriction starts after a latency to a minimum, followed by its redilation. Parameters as initial pupil size, latency and pupillary constriction amplitude were analysed automatically. Up to now the influence of two central nervous drugs were investigated:

1. 11 healthy volunteers had an alcohol intake of 1,2 g/kg*body mass within 1,5 h. During alcohol impairment initial pupil size tended to decrease, latency was extended, and the pupillary constriction amplitude showed a decrease. These effects were reversible after alcohol elimination.
2. 12 healthy volunteers smoked a joint containing 40 mg Tetra-Hydro-Cannabinol (THC) by powdered hashish within 10 min. They reached blood THC levels between 1 and 55 ng/ml 5 min after end of smoking. Initial pupil size tended to decrease (fig. 4), latency

seemed to be unaffected, and pupillary constriction amplitude tended to decrease (fig. 5).

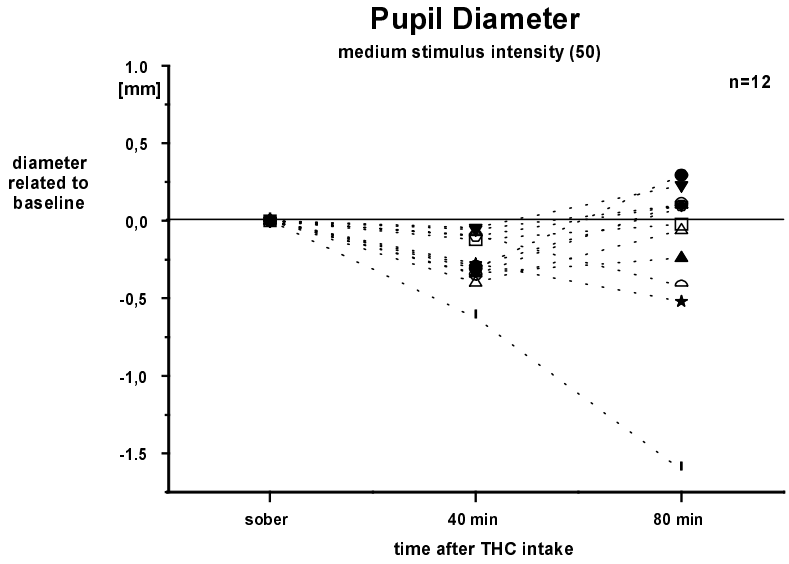

Figure 4: Time course of pupil diameter during THC-load

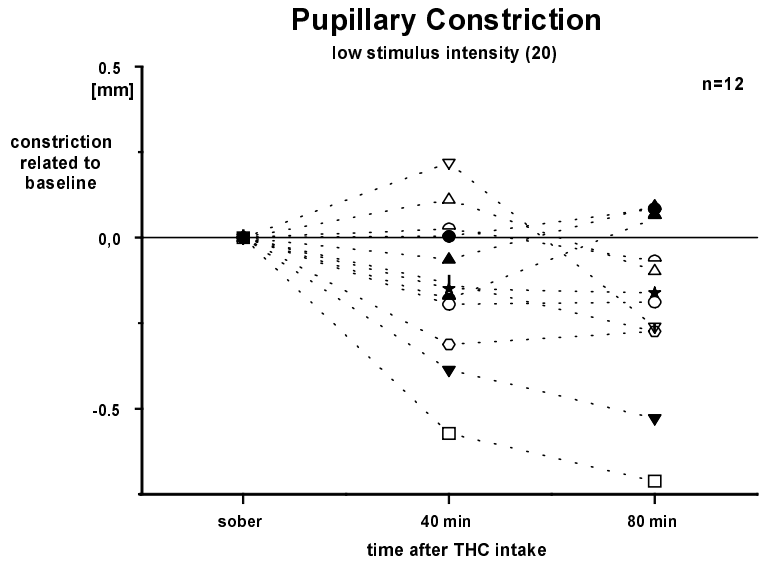

Figure 5: Time course of pupillary constriction amplitude during THC-load

- The dynamics of triggered, i.e. voluntary saccadic eye movements were also measured in these previous studies (1./2. Above). The subjects fixated illuminated diodes on a ridge as fast as possible, the targets (diodes) were positioned in a visual angle of –10, 0 and +10 degree. Measurements were carried out with a time resolution of 250 frames per second:

1. Alcohol-study: Latency of SEM was prolonged significantly, peak saccade velocity (PSV) of SEM was reduced.
2. THC-study: Latency and peak saccade velocity of SEM seemed to be unaffected, but the quality of this voluntary task became worse indicated by an increase of correcting saccades, anticipation and, in conclusion, by a decrease of saccades which could be analysed.

- 14 healthy volunteers were awake over 32 h to investigate possible effects of sleepiness on PLR and SEM. Latency of PLR as well as of SEM was affected unspecifically. Pupillary constriction amplitude tended to increase with sleep deprivation. PSV tended to decrease.

Discussion:
Up to now some studies have been worked out concerning the impairment of two central nervous drugs on dynamics of the pupil, respectively eye movement. The compact integrated pupillograph CIP® (V 7.00 and 8.00) has been used in all these investigations.
At the present, these investigations allow a scientific interpretation of the influence of these drugs on the visual system. But concerning **cannabis** the effects are very small and, there is a need of a baseline value for a reliable interpretation of the measured data. In contrast to that first results of a running study with **ecstasy** and some examinations in front of a disco confirm the impression, that the CIP® as a pretest device for recognition of drug impaired drivers is probably more than a vision.

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