Pupillary responses in normal subjects following auditory stimulation

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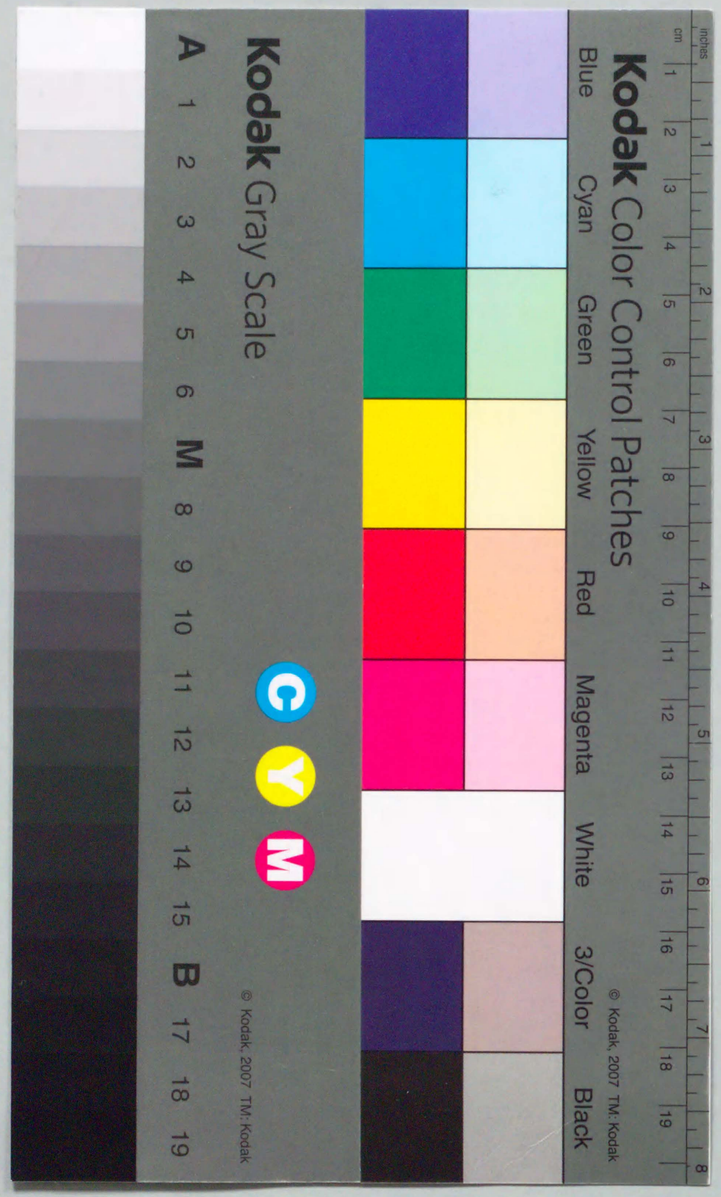

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ORIGINAL PAPER

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Abstract To clarify pupillary responses of humans following auditory stimuli, we studied both eyes of 61 normal subjects using a computed pupillograph. Unilateral auditory stimulation elicited pupillary dilatation in all cases. Pupillary responses were classified according to duration as being either "long" or "short". The duration of dilatation was 1530 ± 320 ms (mean ± SD) in the long-lasting group (n = 45) and 850 ± 250 ms in the short-lasting group (n = 16). The latency time for dilatation was 460 ± 80 ms. Both eyes of each subject showed the same response. Two drops of 10% guanethidine, a sympathetic blocking agent, were applied to one eye of 3 subjects. Although the early phase of dilatation was barely affected, the late phase was inhibited, as seen in long-lasting dilatation. The short-lasting response was unaffected. We conclude that the long-lasting response consists of an early pupillary dilatation due to inhibition of parasympathetic nervous activity and a late dilatation due to excitation of sympathetic activity. The short-lasting response is produced only by inhibition of the parasympathetic component.

Key words Auditory-related pupillary responses
Guanethidine · Autonomic nervous activity

Introduction

Since the pupils are innervated by sympathetic and parasympathetic nerves, their size and movement reflect autonomic nervous function. As a consequence, reflexes such as the pupillary light reflex can serve as a test of autonomic nervous function [1]. The pupillary response following auditory stimulation was first described by Westphal [6] in 1863 and investigated further by Löwenstein and Loewenfeld [3] 100 years later. In further experiments, Loewenfeld [2] studied the mechanisms for dilatation of the pupillary reflex in animal experiments. However, this response after acoustic stimulation has not been analyzed sufficiently in humans, and is thus not used clinically. In the present study we analyzed auditory-related pupillary responses in both eyes of normal subjects. In addition, we evaluated the influence of a sympathetic blocking agent on the response to determine whether or not sympathetic neural activity was involved.

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Materials and methods

A total of 61 normal adult subjects were studied. Thirty-four were males and 27 females, with ages ranging from 21 to 69 years. Auditory-related pupillary responses were measured using a binocular pupillograph [5]. Background illumination was approximately 400 lx. A 1000 Hz tone burst at 100 dB hearing level (HL) was used as the acoustic stimulus. The duration and rise-decay times of each tone burst were 50 ms and 1 ms, respectively, at an interstimulus rate of 10 s. Approximately 70 pupillary responses were examined for each subject by delivering the acoustic stimuli to the left ear. Responses containing such artifacts as eye blinks were omitted, and the remaining 10–40 auditory-related pupillary responses were analyzed with respect to pupillary diameter with the aid of a microcomputer. The average diameter was displayed as the original tracing. The sampling time was 10 ms and the total analysis time was 4.0 s following stimulation.

To determine the effect of delivering an acoustic stimulus of differing intensities on the auditory-pupillary responses, auditory stimuli were presented at 20, 30, 40, 60, 80 and 100 dB to the left ears of 2 subjects.

To investigate the role of the sympathetic nervous system in the auditory-pupillary response, two drops of 10% guanethidine, a sympathetic blocking agent, were placed into one eye of each of 3 subjects. The untreated eye served as control. Auditory-pupillary responses were measured 11 h after the instillation when the effect of guanethidine was maximal [4].

Statistical significance was tested using the unpaired t-test.

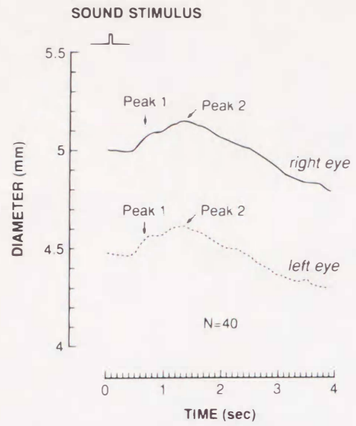

Fig. 1 Tracing showing long-lasting biphasic pupillary responses in a healthy 35-year-old man (subject 1) after 100 dB HL acoustic stimulation of the left ear. Responses are shown for the right eye *(solid line)* and the left eye *(broken line)*. Peak *1* indicates the peak of initial dilatation, while peak 2 indicates that of the second dilatation

Results

All 61 subjects demonstrated a pupillary dilatation response following auditory stimulation. The mean latency time was 460 ± 80 ms (mean ± SD). Pupillary responses were classified according to the duration of dilatation as follows: "Long-lasting" (group 1) and "short-lasting" (group 2) dilatation responses. Long-lasting responses were observed in 45 cases (23 males, 22 females, aged 21–69 years). This response was biphasic in 31 of 45 cases and monophasic in 14. Short-lasting responses were observed in 16 cases (11 males, 5 females, aged 23–65 years). This latter response was monophasic in all cases. The duration of pupillary dilatation was 1530 ± 320 ms in the group with long-lasting dilatation and 850 ± 250 ms in subjects with short-lasting dilatation.

Figure 1 shows the long-lasting biphasic dilatation pattern of the auditory pupillary response obtained in a healthy 35-year-old man (subject 1). The 4 s course of pupillary dilatation in this subject averaged 40 single responses. His pupils began to dilate after a latency period of 450 ms. The reflex curve then reached a peak initial dilatation at 250 ms, while the peak of the second dilatation occurred 1130 ms later, producing a biphasic auditory-pupillary response curve. Pupillary dilatation lasted 2100 ms in this case. The reflex curves of both eyes were almost equal.

Figure 2 shows the short-lasting monophasic dilatation pattern obtained in a healthy 32-year-old man (subject 2). The pupillary reflex averaged 40 single responses and pupils began to dilate after a latency period of 450 ms. The dilatation curve peaked 280 ms later, but with no second peak observed. Pupillary dilatation in this case lasted 700 ms, being shorter than that in the subjects with long-lasting biphasic patterns. The reflex curves of both eyes in this subject were almost equal.

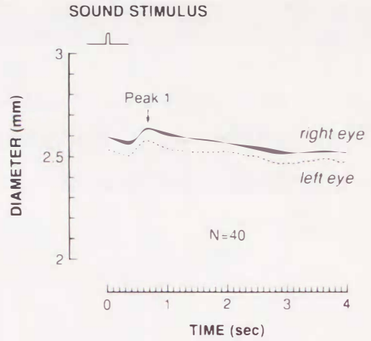

Fig. 2 Short-lasting monophasic auditory pupillary response in a healthy 32-year-old man (subject 2) after 100 dB HL acoustic stimulation of the left ear. Peak *1* indicates the peak of dilatation

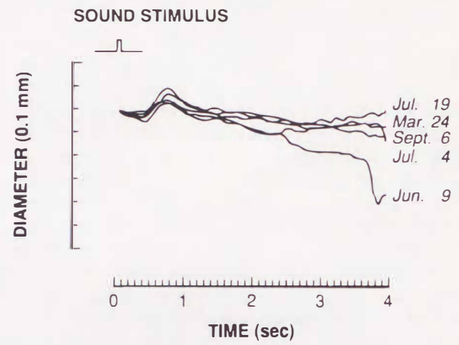

Fig. 3 Reappearance of a short-lasting monophasic auditory pupillary response in subject 2 during repeated testing

The mean latency times for the responses in groups 1 and 2 were 480 ± 100 ms and 460 ± 50 ms, respectively. The mean peak latency time for the initial dilatation was 820 ± 140 ms in group 1 and 800 ± 100 ms in group 2. The mean peak latency of the second dilatation in the long-lasting biphasic dilatation was 1450 ± 220 ms. The latency time for response, peak latency time for initial dilatation, and the age and sex of group 1 subjects did not differ significantly from those of group 2 ($P > 0.05$).

Examinations were repeated in subjects 1 and 2 to determine whether the same reflex patterns would reappear. Figure 3 shows the reappearance of the short-lasting monophasic pattern in subject 2. Testing was performed five times between 24 March and 6 September 1990. In all five tests, the auditory-pupillary responses consisted of a short-lasting monophasic pattern that appeared similar in each test. The duration of these responses ranged from 560 to 760 ms. The reappearance of a long-lasting biphasic pattern was also confirmed in subject 1. Response patterns were also similar in tests performed in the morning and afternoon.

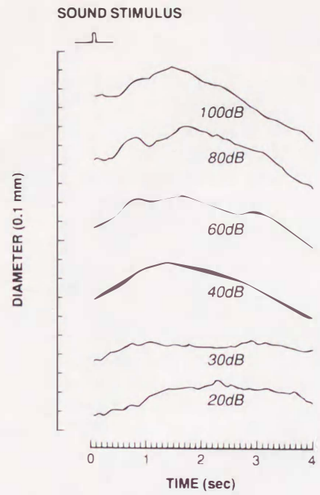

Fig. 4 Effect of differing intensities of acoustic stimulation in subject 1, who exhibited a long-lasting biphasic auditory-pupillary response. No responses were observed at 20 or 30 dB HL, while a long-lasting biphasic response appeared at a level above 40 dB HL

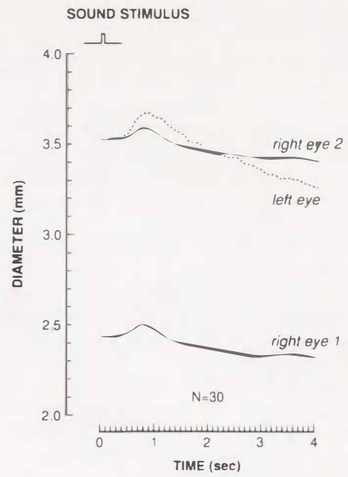

Fig. 6 Auditory pupillary response of a healthy 34-year-old man (subject 3) with a long-lasting monophasic pattern following instillation of 10% guanethidine into the right eye. The scale of the right eye (right eye 2) is placed 0.96 mm higher than that of the original tracing (right eye 1). Only the late phase of the dilatation was clearly inhibited in the right pupil

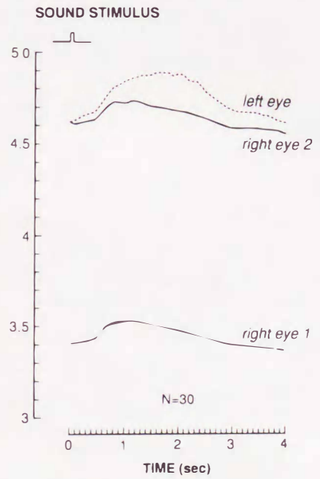

Fig. 5 Auditory pupillary responses of subject 1 with a long-lasting biphasic pattern following instillation of 10% guanethidine into the right eye. For ease of identification, the scale of the right eye (right eye 2) is placed 1.21 mm higher than that of the original tracing (right eye 1). The second dilatation was clearly inhibited in the right pupil

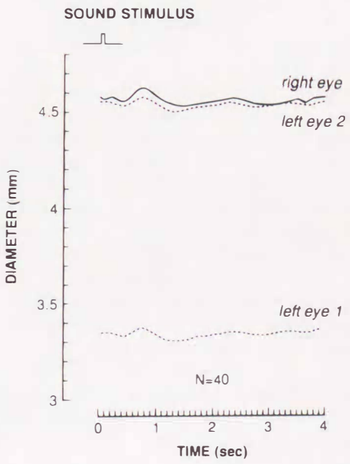

Fig. 7 Auditory pupillary responses of subject 2, showing a short-lasting pattern following instillation of 10% guanethidine into the left eye. The scale of the left eye (left eye 2) is placed 1.20 mm higher than that of original tracing (left eye 1). The auditory response of the left pupil was not affected by the drug, with a similar response produced in both eyes

The pupillary responses to acoustic stimuli of differing intensities were also tested in subjects 1 and 2. Pupillary responses were not recorded clearly in subject 1 for acoustic stimuli of 20 dB and 30 dB HL, but were observed for those of 40, 60, 80 and 100 dB (Fig. 4). These four response curves were long-lasting (1520–2200 ms) and biphasic. A short-lasting monophasic response was

also recorded for acoustic stimuli of more than 40 dB in subject 2.

Figure 5 represents the long-lasting biphasic response obtained 11 h after instilling 10% guanethidine into the right eye of subject 1. His left eye served as control. The right pupil showed miosis in response to guanethidine and produced an anisocoria of 1.21 mm. The initial dilatation of the right eye after the acoustic stimulation was barely affected but the second dilatation was obviously inhibited when compared with the left pupil.

Figure 6 represents the long-lasting monophasic response obtained under the same conditions as in Fig. 5. The early phase of the right response was barely inhibited, but the late phase was obviously inhibited when compared with the left pupil. Figure 7 represents a short-lasting monophasic response 11 h after instillation of 10% guanethidine into the left eye of subject 2. An anisocoria of 1.22 mm was present due to miosis produced by the guanethidine. The dilatation response of the left pupil was barely affected by the drug, so that the response curves of both pupils appeared nearly equal.

Discussion

Loewenfeld [2] reported that auditory stimuli in humans can induce a reflex dilatation of the pupil after a latent period of 0.3–0.5 s. From experiments performed in animals she concluded that the dilatation mechanism of the pupil consists of two parts: (1) contraction of the dilator pupillae produced by sympathetic impulses via the cervical sympathetic chain, and (2) relaxation of the sphincter pupillae produced by central inhibition of parasympathetic discharges from the Edinger-Westphal nucleus. The former is characterized by a relatively fast dilatation and constriction, and the latter by slower, somewhat longer-lasting movements.

If Loewenfeld's theory is applied to the long-lasting biphasic response observed in our present study of healthy volunteers, the initial dilatation would be produced by sympathetic nervous activity to the dilator muscle, and the second dilatation by inhibition of parasympathetic nervous activity to the sphincter muscle. However, in our subject who exhibited a long-lasting biphasic pupillary response, the initial dilatation was barely influenced, while the second dilatation was obviously inhibited by applying a sympathetic blocking agent. In contrast to Loewenfeld's conclusions, our findings indicate that the second dilatation is produced by a sympathetic discharge to the dilator muscle.

It is possible that initial dilatation may not be caused by sympathetic discharge, but rather, by the inhibition of a parasympathetic discharge to the sphincter pupillae. Since the early phase of the long-lasting monophasic response was barely inhibited by a sympathetic blocking agent whereas the late phase was obviously inhibited, this response consists of the same components as the long-lasting biphasic response. The initial and second pupillary dilatations in the long-lasting biphasic response most likely fused to form a long-lasting monophasic pattern.

The existence of short-lasting and long-lasting responses in humans were established as follows: (1) each pattern reappeared on repeated examinations; (2) the same pupillary response pattern was obtained in the same subjects regardless of the intensity of the acoustic stimulus (40–100 dB); and (3) administration of a sympathetic blocking agent influenced the long-lasting response, but not the short-lasting response.

Our present findings have demonstrated a short-lasting and a long-lasting pupillary response to an acoustic stimulus in normal humans. The early pupillary dilatation in the long-lasting response was found due to inhibition of parasympathetic nervous activity, while late dilatation was due to excitation of sympathetic nervous activity. The short-lasting response may be produced only by inhibition of parasympathetic nervous activity.

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