Ocular autonomic function in progressive autonomic failure

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Abstract. Ocular autonomic function was assessed in 4 patients with progressive autonomic failure (PAF) and age-matched control subjects, by measurement of the pupil cycle time, and determination of autonomic denervation hypersensitivity of the iris. Pupil cycle time was abnormal in all patients with PAF; sustained pupil cycling was absent in 5 of the 8 eyes tested of the PAF patients, compared with only 16 eyes from 70 control subjects. Pupil constriction in response to 2.5% methacholine, indicative of parasympathetic denervation hypersensitivity, was significantly increased in patients with PAF (p < 0.001), whilst pupil dilation in response to 0.5% phenylephrine, indicative of sympathetic denervation hypersensitivity, was also significantly higher in the PAF patients (p < 0.001). The results suggest that ocular autonomic function may provide a sensitive early indicator of generalised autonomic dysfunction.

Introduction

Denervation hypersensitivity is defined as an increased response of a tissue (the effector) to a chemical neurotransmitter or agonist after the tissue has been deprived of its nerve supply [1]. This principle may be applied in the assessment of ocular autonomic integrity. Parasympathetic nerves effect pupillary constriction via the sphincter pupillae, and sympathetic nerves effect pupillary dilation via the dilator pupillae. Pupil diameter is easily and accurately measured, and reflects the relative balance of autonomic activity in the anterior segment of the eye. Measurement of pupil diameter after topical application of methacholine, a parasympathetic agonist, and phenylephrine, a sympathetic agonist, can be used to assess denervation hypersensitivity in the eye [2, 3, 4, 5]. These techniques of ocular assessment may be augmented by measurement of edge-light pupil cycle time, a simple and quantifiable way to assess the efferent parasympathetic limb of the pupillary light reflex arc [6].

The aim of this study was to assess and quantify ocular autonomic
function in patients with progressive autonomic failure (PAF) by a series of tests based upon pupillary responses to light, and to autonomic mediators recognised to be effective in the determination of ocular autonomic denervation hypersensitivity.

**Methods**

Ocular autonomic function was assessed in 4 patients with PAF (aged 62, 66, 66, 75 years). They were compared with a control group of 70 subjects (mean age 66.1 ± 8.2 years: range 50–89 years) who were drawn from fit hospital staff and patients attending an ophthalmic casualty department. Pupil cycle time was measured in all 70 control subjects, and autonomic denervation hypersensitivity was assessed in 22 control subjects (mean age 67.9 ± 6.0 years: range 56–76 years). None of the control subjects had any known medical disorder or were taking any medication that might interfere with autonomic function. Any individual eye was excluded if there was a history of disease, trauma, or operations on that eye, or current treatment for any eye disorder. The diagnosis of PAF was made from the clinical history, and results from a standard series of five cardiovascular reflex tests. The tests used were the heart rate responses to the Valsalva manoeuvre, deep breathing and standing up, and the blood pressure responses to standing up and sustained handgrip. We have described the techniques in detail elsewhere, together with normal ranges [7]. The results were grossly abnormal in all four subjects (Table 1). Subjects with known secondary causes of autonomic dysfunction (e.g. diabetes) were excluded. Three of the four subjects presented with postural hypotension, and the fourth subject had symptoms of multiple system atrophy, with postural hypotension, nystagmus, intention tremor, dysarthria, ataxia, bladder problems and impotence. The study was approved by the Local Hospital Advisory Ethical Committee, and each patient agreed to participate after being informed of the details of the tests.

**Pupil cycle time**

This was determined as described in detail previously [6]. The technique involves shining a horizontal slit-beam of light on the inferior margin of the pupil, thereby inducing a cycle of constriction and dilation which can be simply and accurately timed with a stop-watch. The duration of a single cycle of the pupillary reflex arc is represented by the average of 100 cycles and is expressed in milliseconds.