PUPIL CYCLE TIME AND HUMAN IMMUNODEFICIENCY VIRUS (HIV) INFECTION

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SUMMARY

The pupil cycle time (PCT) was measured in 22 HIV-positive patients and 22 age/sex-matched controls. Of the HIV-positive group, 13 (59%) met the Centre for Disease Control classification of acquired immunodeficiency syndrome (AIDS) defining illness. There was a highly statistically significant difference in the PCT between the HIV-infected group and the control group ($p<0.0001$, Student's *t*-test). Within the HIV-infected group there was no statistically significant difference in the PCT between those patients with full-blown AIDS and the others. This study suggests that HIV infection may be associated with subclinical ocular autonomic dysfunction even in the earlier stages of HIV infection.

Subclinical defects in autonomic function have been described in other diseases[1] and subclinical visual dysfunction has also been reported in HIV-positive patients.[2] This study was set up to investigate whether ocular autonomic dysfunction is evident in HIV-positive individuals. Measurement of the pupil cycle time (PCT) represents a simple and repeatable, non-invasive method of estimating autonomic function.[3]

PATIENTS AND METHODS

The study included 22 patients (21 males and 1 female) who were HIV-positive. They were recruited from patients attending the eye clinic for HIV disease in Edinburgh. All patients had a full ophthalmic assessment including corrected visual acuity, visual fields and binocular indirect examination of the fundus. Any patients with abnormalities of the above, in particular cytomegalovirus retinitis or HIV retinopathy, were excluded from the study. Patients taking opiate drugs were also excluded from the study as these might affect the PCT. None of the patients included in the study were taking medications known to affect the autonomic system. Thirteen patients (59%) met the Centre for Disease Control criteria for an AIDS defining illness.

The control group included 22 healthy volunteers (21 males and 1 female) who were age-matched with the HIV-positive group. All volunteers had normal fundi as determined by indirect ophthalmoscopy and at least 6/6 best corrected acuity. The average age of the control group was 30 years (range 25–40 years). This compared closely with the HIV-positive group, whose average age was 31 years (range 25–40 years).

The PCT was measured in the left eye of all patients using the method described by Miller and Thompson.[3] A horizontal slit beam of moderate intensity, 0.5 mm thick, is slowly elevated until it overlaps the inferior margin of the pupil, which then constricts. The iris now blocks out the beam of light and the pupil dilates. Eventually the dilating pupil overlaps the beam of light once again and another constriction occurs, thus setting up a persistent oscillation. The time taken for 100 cycles was measured in each case and this time divided by 100 to give the PCT in milliseconds. Statistical significance was determined by the two-tailed Student's *t*-test.

RESULTS

The results are summarised in Fig. 1. The mean PCT cycle time in the healthy control group was 840 ms (SD 82 ms) with a range of 670–960 ms. The effect of age on PCT was tested in the healthy control group but was found to be not significant. No meaningful result was obtainable in 5 of the 13 patients with full-blown AIDS because their pupils oscillated for only 10 or so cycles before collapsing into irregular jerky pupillary movements or hippus. This also occurred in 2 of the 9 HIV-positive only group.

The HIV-positive group as a whole, including the patients with AIDS, had a mean PCT of 1370 ms with a range from 930 to 2300 ms. There was a highly statistically significant difference in the PCT between the HIV-infected group as a whole and the control group ($p<0.0001$).

For the 8 patients with full-blown AIDS the mean PCT was 1380 ms with a range from 930 to 1850 ms. This result was also highly significantly different from the control group ($p<0.0001$). For the 7 patients who were HIV-positive but did not fulfil the criteria for AIDS the mean

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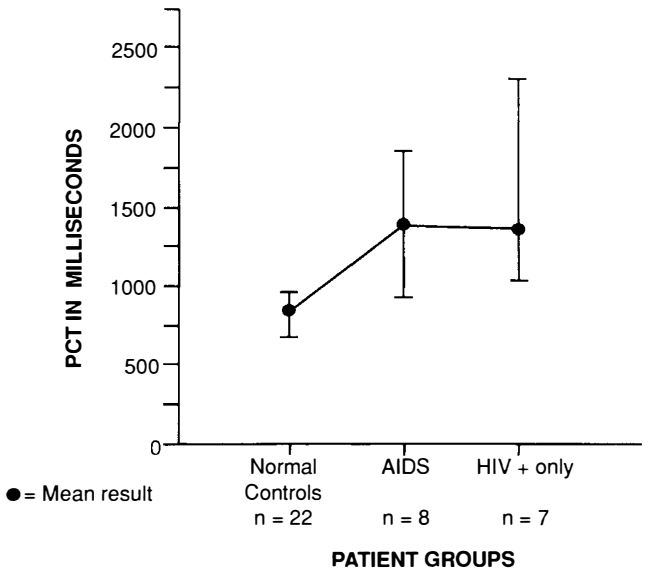

Fig. 1. *High/low graph showing the range of pupil cycle time (PCT) results amongst normal controls, AIDS patients and HIV-positive patients without AIDS. Mean PCT: controls, 840 ms; AIDS patients, 1380 ms; HIV-positive only patients, 1360 ms.*

PCT was 1360 ms with a range of 1040–2300 ms. This result was again highly significantly different from the control group ($p<0.0001$). There was, however, no statistically significant difference in PCT between patients who were HIV-positive only and those who were HIV-positive but had full-blown AIDS ($p = 0.9$).

DISCUSSION

In this study the mean PCT of the healthy control group was determined to be 840 ms and this is similar to the results of other workers. Miller and Thompson[3] found the mean PCT of a control group to be 822 ms while Karacorlu *et al.*[1] reported a result of 820 ms in their control group. Miller and Thompson[3] also commented that only 5% of normal people aged 12–50 years would be expected to have a PCT longer than 954 ms. The PCT offers simple, fast, quantitative measurements of the pupil reflex arc with a high degree of repeatability.

In this study HIV-positive patients clearly exhibited dysfunction in the pupil reflex arc. Moreover, in 7 of the 22 patients the reflex arc was so disrupted that pupillary oscillations occurred for only 10 or so cycles before collapsing into hippus. The PCT for these patients is effectively infinity and thus the high/low bands in Fig. 1 for the AIDS group and the HIV-positive only group are too narrow. For the sake of simplicity in presentation and statistical analysis these patients are not included in the results, but they represent a group of patients whose pupillary reflex arcs are more severely disrupted than those appearing in Fig. 1.

HIV-positive patients who have not developed AIDS appear to have the same abnormality of function in the pupil reflex arc as those with full-blown AIDS, suggesting that the defect is acquired relatively early in HIV infection. When the optic nerve is normal, the PCT is dependent on the innervation and integrity of the iris muscle, and as such is a measure of autonomic function. Recently, however, Tenhula *et al.*[4] have found axonal degeneration in the optic nerves of 8 patients who have died of AIDS and suggested that this may reflect an AIDS-associated primary optic neuropathy. Thus the abnormal PCTs found in this study may be due to this optic neuropathy rather than to an abnormality of autonomic function. However, the stage of HIV illness at which this axonal fall-out occurs is not known. It may also be argued that despite having normal fundi when the PCT was tested, many of these patients may have exhibited HIV retinopathy previously. This fleeting retinopathy represents infarcts of the nerve fibre layer and could conceivably affect optic nerve function. However, HIV retinopathy has been shown[5] to occur mainly amongst patients with CD4+ counts below 100 cells/mm^3 and therefore it would not explain the poor PCT results found amongst patients without full-blown AIDS.

Systemic autonomic dysfunction has been found to be common amongst HIV-positive patients[6] and it seems likely that there is significant ocular autonomic dysfunction as well. Further studies are needed to elucidate the exact nature and timing of the defect found in the pupil reflex arc of HIV-positive patients.

Key words: Acquired immunodeficiency syndrome, Autonomic dysfunction, Human immunodeficiency virus, Pupil cycle time.

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